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A STUDY OF THOMSEN'S DISEASE, BASED ON EIGHT CASES, IN A FAMILY EXHIBITING REMARKABLE INHERITANCE FEATURES IN THREE GENERATIONS.

BY JOSHUA ROSETT, M.D.

Instructor in Neurology, Columbia University.

THE rich literature on inherited abnormalities of the neuro-muscular system is notably poor in information regarding any definite physical traits that might be regularly associated with the particular abnormality in the affected family. The human race is too small in numbers, too slow-breeding and too widely dispersed to permit of easy generalizations regarding the linkage of certain physical types with certain constitutional abnormalities. Lombroso's inferences proved to be too far-sweeping, at a time when the working of Mendelian laws was not understood, to say the least.

The value of accumulating information respecting the association of certain gross appearances of person with specific pathological conditions, is obvious. Certainly five, and not improbably six, out of the eight cases observed in the present instance would have remained unrecognized, if it were not for the marked grouping of the affected family into easily distinguishable physical types. Of nine persons comprising one such group, only one came forward with the complaint of myotonia; but the suspicion attaching to certain physical likenesses led to an investigation, with the result that every one of the eight persons examined proved to be myotonic.

In the sixty or seventy reports on myotonia and paramyotonia, a large percentage of the investigators note the co-existence of psychopathies and of the muscular disorder in members of the same family. The muscular and mental disorders sometimes co-exist in the same individual. Thomsen [41] himself emphatically classed myotonia congenita with the psychoses. In the first generation of the family to be described, the two disorders indeed co-exist in the same person, but in the second generation there is a clear-cut segregation of the two disorders, each becoming associated with a definite physical type of person; three individuals of a certain type become affected with Thomsen's disease, and the other three, of a different physical type, become affected with psychoses. In the third generation the psychosis, as well as the physical type associated with it, are eliminated. Four new types appear, each represented by one individual who has inherited from a respective parent, not a blood-relation of the affected family, that parent's physical type and normal constitution. The rest of the members of the third generation are all of the myotonic type of the second generation, and they are all, with the possible exception of one who has not been studied, affected with myotonia.

The Mendelian phases of the family to be described may help to throw some light upon two of the pathological features of Thomsen's disease—the abnormally large musculature usually associated with it, and the muscular atrophy which is sometimes observed.

Aside from the Mendelian phases, the cases in question have other interesting features. One such feature has been described by Pelz [32]. Of two brothers observed by this investigator, one was affected with a very pronounced form of Thomsen's disease. The other had no symptoms of myotonia, but the presence of the disorder was ascertained in him by eliciting the characteristic myotonic reaction. Three of the nine cases to be described have to this day suffered no physical discomfort from the disease, which they are almost certain to transmit to their posterity.

Finally, two of the cases are interesting in themselves. One suffers from a form of Thomsen's disease which has greatly facilitated the study, and has to a great extent explained the mechanism, of the abnormal muscular action. The other is an instance, no one knows how rare, in which the manifestations of the disorder are evoked by strong psychical stimuli only. If it were not for the fact that this patient is a member of a myotonic family, and that she belongs to a group of persons marked by certain physical characteristics, the examination would have been inadequate, and her trouble would almost certainly have been regarded as a form of hysteria.

In order to accentuate the Mendelian phases in the forthcoming study, it will be convenient to deviate somewhat from the ordinary form of description. The cases will be taken up not in the order in which they presented themselves for examination, but according to generations and to groups formed by the inheritance of certain characteristics. Thus the first generation, which was not personally investigated—the grandparents—will be taken up first. The second generation will be described in two groups: one, the myotonic group; the other, the border-line psychosis group. The third generation, too, will appear in two groups: one consisting of normal persons; the other comprising five individuals affected with Thomsen's disease of widely different grades of severity.

THE FIRST GENERATION.

Neither the man nor the woman was seen by the investigator, the data respecting the couple having been obtained from their children.

William L. was born in Worcestershire, England, where he followed in his youth the trade of needle pointing. Some time after his arrival to the United States he became the owner of a beer saloon. He was a man of large size, weighing about 220 lb., and of powerful build. He had a very fair complexion, dark-brown hair and blue-grey eyes. He was much addicted to drink, but otherwise a cheerful, intelligent, kind-hearted man. He is not known by his children to have suffered at any time from muscular rigidity or cramp, nor from any trouble that could be interpreted as "nervousness." In fact he was a very healthy man all his life. He died from pneumonia at the age of 48, nineteen years ago.

Anna H. L., the wife of William L., was born in Derbyshire, England. In appearance she was of medium stature and build. She had a dark-olive complexion, dark-blue eyes and dark chestnut-coloured hair. She had been a very nervous woman all her life, and in later years suffered from periodic attacks of profound depression of spirits alternating with states of irritability. She "developed" a muscular trouble, which became particularly marked during the last ten or twelve years of her life. In was the occurrence of a cramp or muscular stiffness at times when sudden movements were required. The children particularly remember the following habit: Whenever she travelled in a street car she would rise from her seat while the car was still in motion and at a considerable distance from her destination. If she sat until the car stopped at her destination, the sudden attempt to rise would "bind" her, and the ensuing delay, by attracting to her the attention of the passengers, would embarrass her greatly.

She died at the age of 62, six years ago.

THE SECOND GENERATION.

Of the thirteen children born of the marriage of William L. to Anna, seven died in infancy. The surviving six fall into two groups: the myotonic and the border-line psychosis group.

The Myotonic Group.

Case 1.—Herbert L., aged 33, weight 210 lb. Married and has two children. A garage-man by occupation. In appearance he is a large and powerful-looking man of fair complexion with brown hair and blue-grey eyes. A very healthy man physically, and of the average mental and emotional state. He suffers from a muscular trouble which, however, has not been a source of any great inconvenience. In his business he is sometimes called upon to do heavy lifting. On such occasions his hand becomes "bound" around the object so that he cannot let it go for a number of seconds.

A test of his grip revealed a degree of strength which appeared to be in proportion to his very large musculature. His grasp relaxed easily. He explained, however, that the inability to open his hand occurred only when the grasping action was accompanied by a heavy lifting exertion.

Mechanical stimulation of his muscles by striking them with a percussion hammer resulted in a normal contraction followed by a slow relaxation. This slow relaxation after the cessation of the stimulus was particularly evident in the left biceps and the forearm muscles, and was obtained in a more pronounced form by means of faradic stimulation.

The tendon reflexes were normal.

Case 2.—Louise W. (fig. 1, D), aged 35, weight 228 lb. Married and has given birth to five children, all of whom are living. In appearance she is like her brother Herbert, having the same colour of the skin, hair and eyes. With the exception of occasional pains in the lower limbs and the abnormality to be described, she is in every respect a healthy woman.

She has had one serious illness—an attack of diphtheria at the age of 18, nine months after her marriage. Antitoxin was administered in three doses. Nine days after the onset of the illness she had diplopia, which persisted for four weeks; regurgitation of food through the nostrils, which persisted for six weeks; paralysis of the upper limbs for sixteen weeks; and partial paralysis of the lower limbs (she could move them in bed, but she could not stand up), for eight weeks. Recovery was complete.

Questioned respecting a muscular abnormality, she persisted for weeks in denying the presence of any. The following history was finally elicited :—

At the age of 23, two weeks before the birth of her second child, she had the first attack of a trouble from which she has been suffering ever since. While she was engaged in preparing a meal at the kitchen stove she was badly frightened on seeing her eldest girl, who was then 2 years of age, pulled off a chair by a neighbour's child. As she was about to make an abrupt movement towards the children she suddenly experienced a wave of stiffness run through her. She felt the muscles throughout her body become tense and hard, until she could not balance herself any longer in the erect position, and she fell to the floor "like a log of wood." The rigidity lasted for about three minutes, during which she was perfectly conscious. The muscles relaxed in the course of another minute or two, and she was quite normal again. Ever since then she has been subject to such attacks whenever suddenly excited or surprised.

The writer witnessed one of these attacks in the patient's house. It occurred when an attempt was made to test the electrical reactions of her muscles under rather disagreeable circumstances. On previous occasions the mechanical and electrical tests had given negative results. On one such occasion an ice-pack was applied to one of her upper limbs in order to ascertain whether the chilling of the extremity would have the effect of manifesting the myotonic reaction. Mechanical stimulation produced indeed weakly positive results. On the occasion of the visit to the family's house, an attempt was made to test the electrical reactions under similar conditions. Instead of surrounding the upper limb with ice, it was sprayed with ethyl chloride. The procedure, carried out in the presence of a dozen members of her family, embarrassed her, and she was rather disgusted by the odour of the drug. Upon the application of the faradic current to her arm-biceps, a singular thing happened. A wave of rigidity swept visibly over the upper part of her body beginning at the waist and rapidly involving the shoulders, the upper extremities, the neck and some of the facial muscles. She sat rigid and erect, the head thrown back over the back of the chair, with the upper extremities

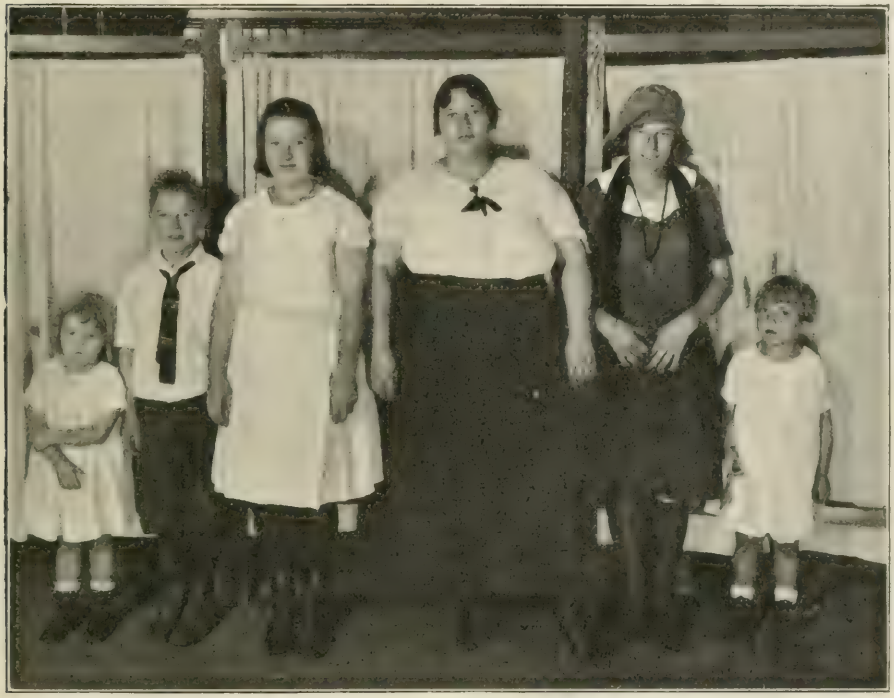


FIG. 1.

extended and semi-abducted. The eyelids were tightly closed and the jaws set. The muscles of her arms and forearms stood out with great prominence, and were of a hard, woody consistency to the touch. But the musculature of the thighs and legs was normally relaxed. She moaned slightly, as if from intense discomfort, and tears came out from between the tightly closed eyelids. In order to ascertain whether she was conscious or not, the faradic current was applied to her arm, and she signified by a louder moan that she felt it. After two or three minutes the rigidity gradually passed away, first in the neck, then in the upper extremities, then in the trunk. The parts attacked first were the last to relax, with the exception of the eyelids, which were still closed. Asked to open them she replied with perfect composure that she would do so as soon as she could, and explained that the eyelids were always last to open in these attacks. She did open them in another minute or so. In the entire procedure there was not the least trace of exaggeration or emotionalism. Her feelings on that occasion, she explained later, were only those of discomfort and embarrassment in the presence of so many members of her family. Questioned respecting the relaxed condition of the muscles of her thighs and legs during the attack, she explained that such was always the case when the attack occurred while she was in a sitting position; but if she happened to be standing the rigidity involved her entire body, including the lower extremities, and then she would fall "like a log."

Apart from these attacks she had no muscular troubles.

There were no other neurological abnormalities in this case.

Case 3.—Sarah E. M., aged 45, weight 223 lb. Married and has one child. Her appearance is very similar to that of her sister Louise and her brother Herbert: she has the same fair complexion, blue-grey eyes and brown hair.

She has never suffered from "nervousness." For a great number of years she suffered from pains in the legs, and they have been weak since she was a young girl, but very much more so of late years. Ever since she can remember, and until a few years ago, she has been subject to the following disability: if she grasped an object quickly she could not retain it in her hand, the fingers would spring back and remain rigid for a minute or so. She was, therefore, compelled to take hold of objects with a certain degree of deliberation.

She has just undergone a major surgical operation, and an examination for myotonia could not be made in her case.

The Border-line Psychosis Group.

This group, consisting of two brothers and a sister, is of interest here mainly on account of its Mendelian phases. A brief account only will, therefore, be given.

The oldest member of this group is Laura C., aged 41. Weight 56 lb. A widow and childless. Of medium stature and build, she has a dark-olive complexion, dark chestnut-coloured hair and deep blue eyes. She has been a very "nervous" woman all her life. She is subject to attacks of profound depression, alternating with states of irritability, "just like mother." She has, besides, attacks during which her lower limbs are cold and numb, especially at night, irrespective of the surrounding temperature.

She has never had any muscular trouble.

Electrical and mechanical tests of her muscles gave negative results.

The second member of this group is William L., junr., aged 36. Weight 145 lb.; carpenter by trade. In appearance he is very much like his sister Laura —, of medium stature and build, with a dark olive complexion, dark-chestnut-coloured hair and deep blue eyes. He married twice and has two children, one by each wife.

Two or three times a year William has attacks of "nervousness" of about two weeks' duration. During these attacks he is "out of his mind"—does not work, wanders about aimlessly and talks a great deal and quite incoherently, repeating the same sentences over and over again. During a recent attack he appeared at his sister Louise's house—a distance of about five miles—at 3 o'clock in the morning. He shows no tendency to commit violence during these periods of disorientation. In the lucid intervals he is a good, steady workman and a devoted husband and father.

He has never had any muscular trouble, and electrical and mechanical tests of his muscles revealed nothing abnormal.

The third member of this group is Harry L., aged 23. Weight 150 lb. Unmarried and a clerk by profession. In appearance he is like the two preceding members of this group, having the same colour of the skin, eyes and hair.

He suffers from "general nervousness," a perpetual feeling of uneasiness in the presence of people, a sense of inferiority. He is shy and awkward in all things. He has had headaches as long as he can remember. He has refused profitable employment for the last twelve months, being held back by some power for which he cannot account, and attempted suicide in a fit of despondency. "I strive for the higher things in life, but I cannot get a move on myself toward their attainment. I have no push. I cannot put myself forward. This makes me at all times down-hearted and at times despondent. I am just like mother used to be. You can tell by the way I speak the kind of a chap I am." One could indeed to a certain extent. His speech had a peculiarly slow quality, which appeared to be due not to any defect of the motor apparatus of speech, but to one of the mental processes corresponding to it. His responses were hesitant, as if from an over-anxiety to say exactly the right thing while labouring under the conviction that he was about to say exactly the wrong thing.

He has never had any muscular trouble, and electrical and mechanical tests of his muscles showed them to be normal.

THE THIRD GENERATION.

This generation is represented by ten children, as follows:—

Herbert, of the myotonic group, has two children. Both resemble him in appearance, and the elder, who was examined for myotonia, was found to have it. The other was not examined.

Sarah E. M., of the myotonic group, has one child. In appearance this child resembles the father, who is not a blood-relation of the affected family, and he has neither muscular nor mental trouble.

Louise, of the same group, has five children. Four out of the five are of their mother's physical type and are affected by myotonia. The fifth, a girl, resembles her father, who is not a blood-relation of the family, Like her father, the girl is in every respect normal.

Laura and Harry, of the border-line psychosis group, have no children. William, of the same group, has two. They were not seen by the writer, but according to information furnished by the relations, the children look like their respective mothers—William having been married twice and each of his wives having given birth to one child. Like their mothers, who were not blood-relations of the family, the children have neither muscular nor mental trouble.

The third generation, then, falls into two groups: the normal and the myotonic. Of the five normal persons, two were examined, and one will suffice as an example. It is Estelle (fig. 1, E), the oldest child by the marriage of Louise and Frank W. She is 14 years of age, of a rather slender, athletic build. Like her father, the girl has a light olive complexion, green-blue eyes and red-brown hair, and presents neither muscular nor mental trouble.

The Myotonic Group.

Case 4.—Lorraine L., aged 7, is the elder daughter of Herbert L. She resembles her father in features, and in the colour of her skin, eyes and hair.

The child is well in every respect; her relations have not noticed any muscular abnormality.

Examination showed her movements to be normal. Mechanical and electrical stimulation of her muscles resulted in a normal contraction succeeded by a slow relaxation. The myotonic phenomenon was particularly marked in the right biceps and to a less degree in the other muscles of the same arm. The result of faradic stimulation was in this respect more definite than that of mechanical stimulation.

The tendon reflexes were normal.

In order to avoid repetition, the following may be said respecting the four cases of this group next to be described. All four, the children of Louise W., have certain physical characteristics in common. In appearance they all resemble their mother, as may be partly judged from the family photograph (fig. 1), in their facial characteristics and in the colour of their skin, their eyes and their hair. The last, however, varies in shade according to age, the hair of the younger members being of a lighter shade than that of the older. Thus the mother's hair is dark brown, while the children's hair varies from a golden brown in the older (Mildred), to a simple light brown in the youngest. The golden quality is said to be due to sunburn. Notwithstanding the difference in shade, however, the essential colour is the same in this group, and is distinctly different from that of the other groups. They all appear to have rather bulky muscles, but judgment in this respect becomes difficult when dealing with very young children.

Case 5.—Mildred W. (fig. 1, C), 12 years of age. She was the first of the series to present herself for examination. She was brought by her mother to the Neurological Division of the Vanderbilt Clinic on August 22, 1921, with the following history :—

The teachers of the public school which she attends complained to the parents that the girl, though sensible and obedient, behaved in a manner which introduced a certain amount of disorder into class discipline. She lacked the necessary promptness of action. She was the last to be on her feet when the order was given for the class to rise. She was the last to comply with the command of the teachers to put the pencils down on the desk, or to close the books. Ordered to recite, she was silent for a number of seconds ; yet once she began, she proceeded smoothly. This initial retardation was especially evident in her physical exercises. A repeated command, or one uttered in an angry voice, made matters only worse, she retarded even more. Exhortation being of no avail, the teachers suspected a physical or mental defect and informed the parents.

The mother furnished the following data :—

Mildred is her second child. She was born at term, after a prolonged and difficult labour which was terminated, however, without the aid of forceps. The baby weighed 7 lb. at birth and appeared normal in every respect. She was breast-fed, cut her teeth at 7 months, said "papa" and "mamma" at 10 months and began to walk at 14 months. Her general health in childhood was very good. She had chicken-pox and measles and, at the age of 6, diphtheria without complications. She began to attend school at the age of 5, and she is at present in the 6th Grade, Grammar School, which is the normal grading for her age. She first menstruated a month ago.

Although the child began to walk at the normal period, it was soon noticed by the parents that she stumbled and fell a great deal. Later it was noted that she was reluctant to run about with the other children at play. Urging and scolding on this point having proven to be ineffective, the parents became reconciled to the condition.

Upon being questioned, Mildred stated that her tardiness at the beginning of movements is due neither to an inability to understand the meaning of a command, nor to lack of desire on her part to fulfil it, but to a rigidity of the musculature involved, which supervenes the moment she attempts the particular movement. As a matter of fact the more anxious she is to carry out the movement promptly the greater is the rigidity which sets in, and the longer, therefore, is the retardation. Thus an angry or a repeated request on the part of the teacher, making her more anxious to comply, has exactly the opposite effect from that which is intended. Yet once the rigidity of the part wears off, she performs the movement without any difficulty. What is true of her movements in compliance with a command, is true also of the movements initiated of her own volition. She has much difficulty in ascending the first flight or two of stairs, but once she has climbed these she can climb the rest without any difficulty. While she is sitting in a chair, her muscles are perfectly lax, but the moment she attempts to rise they become rigid, and the rising movement is, therefore, executed clumsily. While she stands, she feels that her muscles are in a normal condition, but the moment she wishes to walk her muscles stiffen. After walking a few steps, however, the movements become normal. When she closes her eyelids tightly, she has difficulty in opening them for a number of seconds. If she presses her tongue against the palate, she feels it become rigid. The first movements of flexion and extension of the forearm at the elbow, with the hand relaxed, are a little difficult, but the succeeding movements are easy. But if she attempts to perform the same movements with the hand closed in a fist, flexion and extension of the forearm become more and more difficult, until after a few repetitions movement becomes impossible: the forearm remains semiflexed at the elbow, while the fingers half-open, and point in all sorts of directions in a grotesque manner from a contracted palm of the hand.

What is true of movements initiated of her own volition is likewise true of those which occur independently of her will. Thus, when she is suddenly and unexpectedly pushed from behind, she falls to the floor in a rigid mass. If she sneezes, her eyelids remain closed and she cannot open them for a time.

The girl is large, very muscular and powerful-looking. Weight 121 lb. All the subjective symptoms elicited on questioning were found to be true by objective examination, and need not be repeated. The peculiar behaviour of the movements of flexion and extension of the forearm upon the arm, which is apparently anomalous in Thomsen's disease, will be considered in the discussion as elucidating the mechanism of the abnormal muscular action. The reflex behaviour of the muscles was tested in several ways. The girl was made to sneeze (the administration of snuffing tobacco provided an excellent diagnostic agent) and her eyelids remained contracted for thirty seconds, during which she was making strenuous efforts to open them by the action of the frontalis muscle.

When a muscle was tapped with the percussion hammer, it contracted promptly and normally; the marked deviation from the normal being the slowness with which the muscle relaxed after the cessation of the stimulus. The degree of muscular contraction and the length of time taken by the subsequent process of relaxation were in direct proportion to the strength of the blow and to the number of rapidly repeated blows. The table below gives the approximate number of seconds taken by the particular muscle or group of muscles to relax, after contracting in response to the stimulus of one, two and three moderate blows dealt in rapid succession with the percussion hammer.

	One blow	Two blows	Three blows
Right arm-biceps	10 seconds	15 seconds	20 seconds
Left arm-biceps	15 ,,	25 ,,	30 ,,
Right supinator longus	7 ,,	10 ,,	13 ,,
Left supinator longus	5 ,,	7 ,,	10 ,,
Right anterior forearm muscles	7 ,,	10 ,,	13 ,,
Left anterior forearm muscles	3 ,,	5 ,,	8 ,,
Right posterior forearm muscles	3 ,,	6 ,,	10 ,,
Left posterior forearm muscles	3 ,,	6 ,,	10 ,,
Right triceps	7 ,,	10 ,,	15 ,,
Left triceps	10 ,,	13 ,,	17 ,,
Pectorals	4 ,,	6 ,,	10 ,,
Sternomastoids	5 ,,	7 ,,	10 ,,
Posterior leg muscles	5 ,,	7 ,,	10 ,,
Peroneal muscles	5 ,,	7 ,,	10 ,,
Right thenar muscles	7 ,,	10 ,,	12 ,,
Left thenar muscles	7 ,,	10 ,,	12 ,,
Right hypothenar muscles	3 ,,	5 ,,	8 ,,
Left hypothenar muscles	3 ,,	5 ,,	8 ,,
Tongue	Not definite	3 ,,	5 ,,

The length of time taken by the muscles to relax after the cessation of the stimulus varied in a striking manner with the season of the year and the general condition of the patient's health. The table above held true for the moderately warm weather early in the autumn and a generally good state of the patient's health. With the onset of colder weather, and during slight indispositions, the relaxation time of the muscles was very much prolonged, in some instances doubled.

Stimulation with a faradic current of moderate strength produced the same effect as striking the muscles with a hammer, and the figures need not be repeated. Erb's classical reaction was not obtained in full.

What was true of a given number of blows of a certain strength was likewise true of a smaller number of blows of greater strength. Thus one strong blow produced the same effect as two or three gentler blows. And the same held good for faradic stimulation.

The superficial reflexes were normal. The radial, ulnar, wrist, suprapatellar and Achillis reflexes could not be obtained, and a slight patellar reflex was obtained only with much difficulty.

The muscular strength, although good throughout, was not so great as one would expect considering the very large size of the muscles. Sensation was normal. The internal organs were apparently healthy. There was a trace of albumin in the urine, which was otherwise normal. The blood Wassermann test, done in order to exclude a possible complicating circumstance, was negative.

The patient was seen a number of times during the late summer, throughout autumn and the beginning of the winter. All the symptoms became exaggerated to an astonishing degree with the onset of cold weather. The movement of rising from a sitting position and the first steps were clumsy late in the summer. In the beginning of the winter she would rise from a sitting position with a sliding and turning movement, as if she had been glued to the chair; her first steps were made with the thighs and knees semiflexed, and it was not until she had walked for two or three minutes that her gait approximated the normal. She began to suffer with pains in her thighs and legs which were so severe that they interfered with sleep.

Case 6.—Edward W. (fig. 1, B), 10 years of age. His birth was difficult but no instruments were used. Development normal. He had otitis media at the age of 6 months, measles at 2 years of age and pertussis immediately after. During the attack of pertussis circumcision was performed on account of some complication. At the age of 3 he developed diphtheria; antitoxin was administered, but post-diphtheritic paralysis of all four extremities occurred, lasting for nine weeks. Recovery was apparently complete.

The boy attends a public school and is quite bright at his studies. No symptoms of any muscular abnormality have been observed either by the family or by the teachers.

Upon examination the movements in response to commands were carried out normally, but mechanical and faradic stimulation of the muscles showed a persistence of the contraction after the cessation of the stimulus. The abnormality was particularly marked in the biceps, the supinator longus and the thenar muscles on both arms. Faradic stimulation was more effective in eliciting the abnormality than mechanical stimulation. The tendon reflexes were normal.

Case 7.—Mabel W. (fig. 1, F), aged 5. Instrumental delivery. Development normal. No diseases of childhood.

For some time it has been noticed that after the child sneezes her eyelids remain closed for a number of seconds, and that she remains hesitant when urged to perform a sudden movement. This is particularly marked when getting off a street car, just as in the case of her grandmother. On such occasions her legs remain "bound" for a time, so that she has to be supported or carried out.

Physical examination revealed the symptoms and signs of Thomsen's disease. When the child was asked to close and open her hand repeatedly each successive movement became more difficult, so that after a few movements the fingers remained extended upon the contracted palm, pointing in different directions. If she persisted, however, the difficulty was soon overcome, and the subsequent movements were normal. The following myogram (fig. 2) shows clearly the behaviour of the anterior muscles of the forearm in the attempt to open and close the hand repeatedly. Made to sneeze, the eyelids remained closed for a number of seconds.

Mechanical and faradic stimulation of the muscles revealed a persistence of the contraction beyond the time during which the stimulus was applied. The phenomenon was especially marked in the arm-biceps, the supinator longus, the muscles of the thenar and hypothenar eminences and the calf muscles on both sides.

In every other respect the child appeared to be quite well and normal.

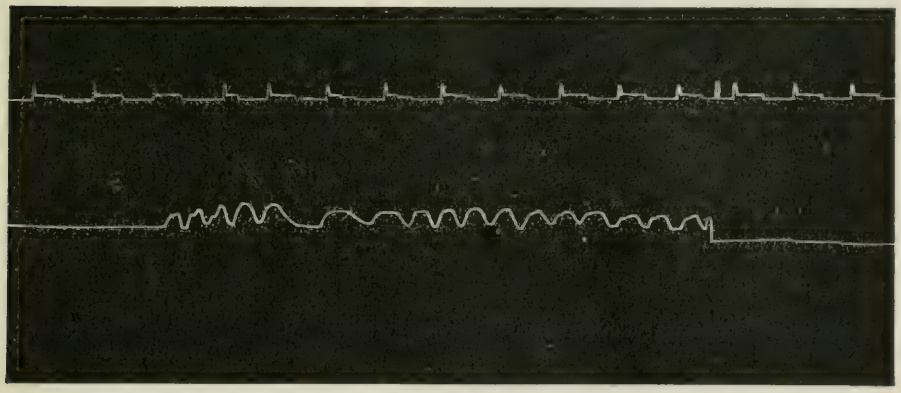


FIG. 2.—(*Case* 7.) Anterior forearm muscles in the attempt to open and close the hand repeatedly.

Case 8.—Nathalie W. (fig. 1, A), 3 years and 6 months of age. Instrumental delivery. Development normal. No symptoms of Thomsen's disease.

Gentle tapping with the percussion hammer and weak faradic stimulation gave indefinite results. Stronger stimulation was not practicable in the case of the young child. The administration of snuff proved to be a valuable diagnostic measure; after sneezing, the child's eyelids remained tightly contracted for some seconds, and then opened very gradually in the course of ninety seconds, the orbicularis standing out with peculiar prominence. The tendon reflexes were normal.

THE MECHANISM OF THE ABNORMAL MUSCULAR ACTION.

This was studied to advantage in the movements of Mildred's (Case 5) upper limb.

With the hand and fingers relaxed, the patient had some slight difficulty in going through the first few movements of flexion and extension of the forearm upon the arm. The first movement was quite normal, the second slightly difficult, the third, fourth, and fifth progressively more difficult, the sixth less difficult, the seventh still less so, the succeeding movements being normal. The myograms reproduced in figs. 3, A and 3, *B* were taken from the patient's biceps.

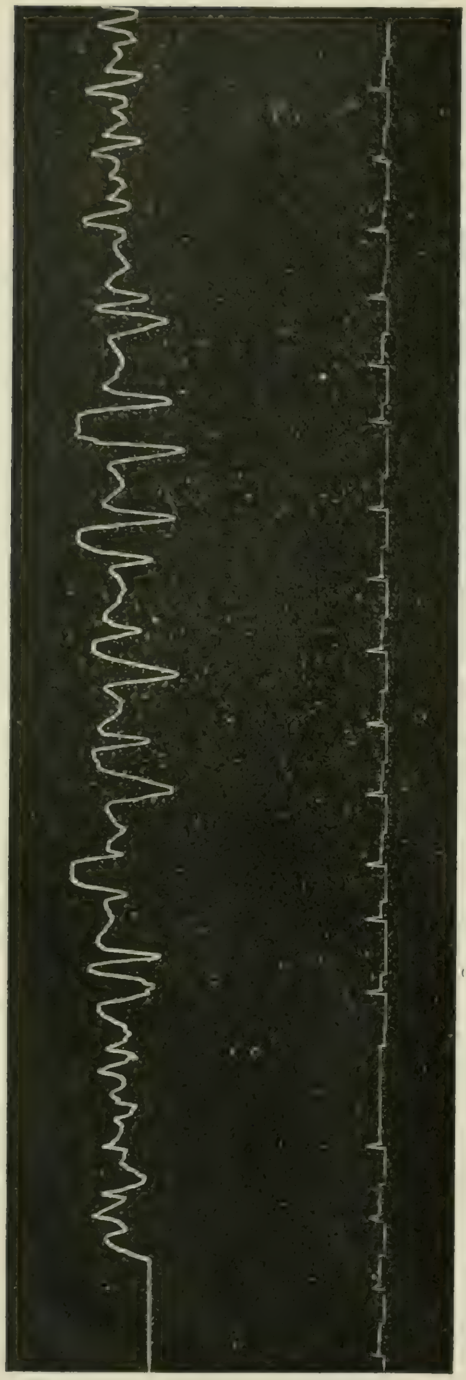


FIG. 3, A.—Mildred W. (*Case* 5). The behaviour of the biceps in the action of flexion and extension of the upper limb at the elbow with the hand relaxed.

When, however, flexion and extension of the forearm at the elbow were performed with the hand closed in a fist, the curve was never completed; the retardation increased until the movement ceased (fig. 3,B). Each succeeding movement was more and more difficult until after four or five repetitions the forearm remained semiflexed upon the arm, the fingers being opened and extended in different directions upon a contracted palm. The entire musculature of the upper extremity was contracted, the individual muscles standing out prominently.

A somewhat similar instance has been described by Wichmann [44], who considered it "a fluke of Thomsen's disease." Martius and Hansemann [25] have observed an analogous phenomenon in a case of paramyotonia; and Pelz [32] cites a case of Weichmann's, in which a tonic spasm occurred after forced movement.

The seeming discrepancy of this phenomenon with the general tendency of the movements to become normal after a few repetitions throws a good deal of light upon the mechanism of the muscular action in this disease. The facts in connection with this phenomenon will, therefore, be taken up in greater detail.

When the patient's arm biceps was gently tapped with the percussion hammer, the response by a contraction was quite normal. The subsequent relaxation, which in the case of normal muscles follows immediately after the momentary contraction, was in the case of the patient gradual, extending over a number of seconds. If, after the muscle was completely relaxed, it was tapped again, the same phenomenon was repeated. If, however, the muscle was tapped while it was still contracted, the subsequent response was a seemingly greater contraction. By tapping the muscle, say six or eight times in rapid succession, it became contracted into an irregular, angular mass, of a woody consistency to the touch, and the patient complained of a pulling pain in the bicipital fossa. What happened was a simple summation of the preceding residual contractions. The succeeding relaxation then took a considerably longer time.

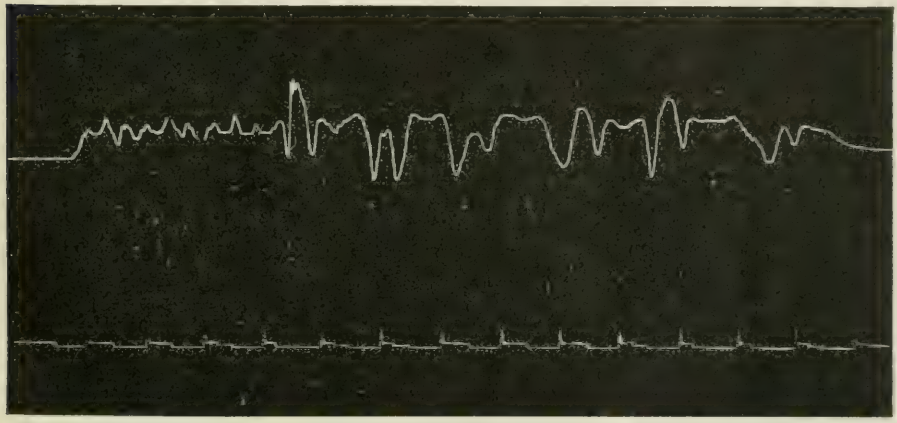


FIG. 3, B.—The same with the hand closed.

When the biceps and the triceps were alternately struck in rapid succession, the biceps did not contract into an irregular ball. After a few blows the forearm remained semiflexed upon the arm and the biceps muscle, although very firm to the touch, retained its regular belly-shape. This muscle was obviously held back from contracting into a ball by the persistent pulling of the opposing triceps.

It made no difference by what stimulus the action of the muscle was evoked, whether by tapping with a hammer, or by an electric current, or by volition or emotion, the resulting abnormal phenomenon was always the same—a persistence of the contraction beyond the duration of the stimulus and, in the case of a stimulus repeated in rapid succession, a simple summation of the residual contractions.

It is not an easy matter, however, to bring a volitional or an emotional stimulus to bear upon any single muscle, as may be done by the tap of a hammer, or the application of a faradic terminal. Unless the forearm is thoroughly supported, a request to contract the biceps, except in the case of a few especially gifted persons, will result inevitably in the contraction of a number of muscles, including some of the antagonists. For this there are two reasons. One is that in the habitual movement of flexion at the elbow, all the muscles passing over the anterior aspect of that joint take part. The other reason is that in order to enable the biceps to exert a measured pull upon the forearm the arm is fixed at the shoulder joint by all the muscles passing over that joint, including the antagonistic triceps.

We shall presently see how these facts furnish a clue to the entire mechanism of the abnormal muscular action in Thomsen's disease in all its varied aspects.

Let this be borne in mind that what is true of the necessity of fixing the shoulder joint in the movements of the forearm upon the arm, is true as well of the necessity of the fixation of any proximal part for the purpose of moving a distal segment to which it is immediately or mediately linked. Thus, in order to make a fist, the elbow and the shoulder joints must be fixed in any position of the upper extremity, except perhaps in the perpendicularly downward position. In order to move the upper part of the trunk, the muscles of the lower part of the trunk are contracted, thus converting a number of the lower vertebræ into a solid column from which the attached muscles can exert a pull upon the upper vertebræ. Since the larger muscles pass over more than one joint, it follows that the contraction of such a muscle may subserve two purposes simultaneously: one, the movement of the distal segment; the other, the fixation of the proximal segment.

When our myotonic patient is requested to make a fist and then to flex and extend the forearm upon the arm, she begins, therefore, these movements with the musculature of the upper extremity already in a state of partial contraction. When a normal person, under similar conditions, flexes the upper limb at the elbow, the extensors, contracted for the purpose of fixing the forearm at the elbow and the arm at the shoulder, relax in correct proportion to the contraction of the flexors. In the myotonic person, however, the contracted extensors do not relax with sufficient despatch. The force exerted by the flexors in order to raise the mere weight of the forearm must be greater than normal by the amount necessary to overcome the pull of the opposing extensors. This is accomplished by sending a stronger volitional stimulus to the flexors, and the patient may be plainly seen to exert the volitional effort. The resulting greater contraction of the flexors, however, is succeeded by their slower relaxation. In the next succeeding movement of extension, the muscles engaged in that movement are called upon to work against the force of the tightly contracted flexors.

A succession of movements of flexion and extension, brought about by muscles which are already contracted for the purpose of fixing the segments of the limb (the hand being closed in a fist), results, therefore, in the myotonic person, in something more than a simple summation of the residual contractions. We have here a system of mutually aggravating conditions, and the residual contractions of the antagonistic groups of muscles are accumulated in a geometric ratio.

Thus, considering the manner in which the residual contractions are summated in the biceps and triceps in the alternate contractions of these muscles, the greater the amount of residual contraction of the triceps the greater must be the contraction of the biceps in order to move the forearm through a given angle. The subsequent residual contraction of the biceps is greater, therefore, in amount than it was in the case of the triceps. When the triceps is now called upon to extend the forearm, the amount of force which it must exert is greater than that exerted by the biceps in flexing it, and the subsequent residual contraction greater now than at the beginning. The amount of force which the biceps must exert in flexing the forearm the second time must, therefore, be greater than that exerted in flexing it the first time.

The result of the geometric summation of the residual contractions of opposing muscle groups, is that after a few movements of flexion and extension the entire musculature of the limb is contracted to its utmost capacity. Every segment then remains in a position between flexion and extension.

It is almost certain, however, that if the patient could overcome the rigidity and flex and extend the forearm a few more times, the succeeding movements would become easier and finally normal. This is the case with every other movement of Mildred and with the same movement when performed by her sister Mabel (Case 7). What happens in the particular instance may be likened to the case of a traveller who, having climbed a hill, is so exhausted near its summit that he cannot surmount it and cannot, therefore, get to the other side where travelling is easy.

In view of our ignorance of the ultimate causes of muscle contraction, it would be useless to speculate upon the reasons for the diminution and the final disappearance of the residual contraction of the myotonic muscles upon the repetition of the movement in which they are engaged. Thomsen ascribed the abatement of the rigidity upon repetition of the movement to a concomitant rise in the temperature of the active muscle. Considering the effect of temperature upon chemical processes and upon the phenomena of osmosis and of surface tension, as well as the fact that all conditions of muscular rigidity are lessened under the influence of a higher temperature, Thomsen's assumption may not be far from the truth.

The mechanism of the rapidly accumulating residual contractions of opposing muscle-groups accounts for the sudden falling "like a log" of some myotonic patients under the influence of sudden strong psychic or emotional stimuli. Cases 2 and 5 are examples of such patients. Such instances have been described by Charles Bell [3] as early as 1837, before the disease was recognized as a definite entity. Thomsen speaks of the effect of psychic stimuli upon the myotonic person as follows: "When a psychic impression awakens the muscular cramp, whether it is fright . . . a friendly blow on the shoulder from behind, or when the foot strikes against an unexpected stone, or when a sudden noise reaches the ear, a painful feeling shoots through the entire voluntary musculature, like an electric current. Every affect is exaggerated in the susceptible disposition, fright and anger as well as joy."

The effect of a sudden strong psychic or emotional stimulus is to fix every proximal segment of the body and the limbs preparatory to any possibly desired movement of the distal segments. Throughout the vertebrate and a large part of the invertebrate kingdom, this fixation of the proximal body-segments may be observed in the act of "priming," which precedes the movements of aggression or escape. In man, under normal conditions, the widespread effect of a sudden strong emotional stimulus upon the general musculature of the body is little noticed: the general stiffening is usually of momentary duration; and where the duration is longer the rapidly alternating contractions and relaxations of antagonistic muscles are exactly timed, constituting a perfectly co-ordinated system. Such is not the case in Thomsen's disease. In this disease there occurs, as we have seen, an overlapping of the contractions of alternately acting antagonistic muscles. In the rapid series of such alternating contractions of numerous antagonistic muscles which constitutes the act of "priming" there must occur, therefore, in the myotonic person a rapid accumulation of the residual contractions. The result of such an accumulation is that in a few moments the muscles become contracted to their utmost capacity and the person, no longer able to perform the fine balancing movements necessitated by the erect position, falls "like a log." In the instance of a similar attack described (Case 2), the parts of the patient which were thoroughly supported escaped rigidity. Since the muscles of these parts were not at work at the time, there was no basis for the formation of a series of mutually increasing residual contractions of antagonistic muscle-groups.

It will be remembered that the amount of *residual* contraction is in direct proportion to the degree of contraction; and that the degree of contraction is in direct proportion to the intensity of the stimulus. This explains the reason why in the instance of Case 1 the hand became "bound" only when the act of grasping was accompanied by that of lifting. The stronger stimulus determined to the muscles engaged in the double exertion of lifting and of grasping, made the myotonic condition of those muscles manifest where a weaker stimulus was inadequate.

The mechanism of mutually increasing *residual* contractions of antagonistic muscles differs essentially from Brissaud and Bauer's [6] explanation of the abnormal muscular action by a "synergic contraction of the antagonists." In the light of this mechanism, Jaquet's [18] theory of the irradiation of the nervous impulse to opposed muscle-groups is untenable. Johnson and Marshall's [20] idea of a block in the pyramidal system as the cause of the trouble is inconsistent with the symptomatology of the disease. From these authors' description it does not appear that they found in their cases either the sign of Babinski, or exaggerated deep reflexes, or abnormal associated movements, or a persistent hypertonus of the resting muscles, or any of the signs of interruption of the pyramidal path. Such signs have not indeed been mentioned by any writer as part of Thomsen's disease, nothwithstanding the fact that Thomsen himself thought the disease to be due to a defect of volition. The intactness of the pyramidal system in this disease is fully attested both by the absence of the signs just mentioned, and by the readiness with which a given set of muscles responds to the impulse of volition. Yet contract as it may, a muscle cannot move the part to which it is attached if that part is held back by an equivalent or by a greater force; and the retardation of movements in Thomsen's disease is not due to any tardiness of the muscles in contracting, but to the resistance offered by the unrelaxed antagonists.

Hoffmann [15] mentions a number of theories brought forward by different observers to explain the singular affection, and there is no need for repeating them here.

THE BEARING OF HEREDITY ON THE LARGE MUSCULATURE ASSOCIATED WITH THOMSEN'S DISEASE.

The distinctive features of the pathological state, as demonstrated by Jacoby [17], Schifferdecker [34], Dejerine and Sottas [8], Pelz [32], Johnson and Marshall [20] and others, are the great thickness of the fibres of the voluntary muscles, the great number of nuclei which are also found within the sarcoplasm and, in some cases, an increase of the interstitial tissue. Jacoby made the interesting statement that "it is obvious that a considerably larger number of embryonic sarcoplasts must have entered into the construction of each individual fibre than is the case in normal development."

It is certain that although Thomsen's disease does occur in persons with a musculature of average size, such an occurrence is quite exceptional. Assuming that the size appeared normal in the cases where no mention is made of it, the number of myotonics with muscles of ordinary bulk must still be quite small. By far the greater number of writers on Thomsen's disease speak of the large size of the musculature of the persons affected by it. Westphal [43] considered the disease to be "a singular congenital anomaly of muscle tone connected with an unusual increase of volume." Mills [26] tried to account for the large size of the muscles by "the frequently repeated, forced exercise."

A study of the family in question furnishes the following facts regarding the association of myotonia with a large musculature:—

The first male, who was not myotonic, had a large musculature; while the first female, who was myotonic, had muscles of the average normal size. Of their six surviving children, three have large and three average-sized muscles. Those with large muscles are myotonic, while those with muscles of normal size are not. A glance at the respective weights of the six members of the second generation tells the story. The weights are as follows :—

Myotonic group	Non-myotonic group
Sarah, aged 45, weight 223 lb.	Laura, aged 41, weight 156 lb.
Louise, ,, 35, ,, 228 ,,	William, ,, 36, ,, 145 ,,
Herbert, ,, 33, ,, 210 ,,	Harry, ,. 23, ,, 150 ,,

Of the ten members of the third generation, four have no myotonia and their musculature is of normal size; while five who are known to be myotonic show a tendency to a large musculature. Another shows the same tendency, but has not been examined for myotonia. In the case of the younger children, however, it is difficult to form a positive opinion as to the size of the muscles, and one judges largely from general impressions, which may a few years hence prove to have been wrong. But there is no doubt whatever in the case of the oldest myotonic member of the third generation, Mildred (fig. 1, C). She is 12 years of age, has very large muscles and weighs 121 lb.

With the exception, then, of the one child who has not been investigated, it may be said on the whole that those of the descendants who have inherited the first male's large musculature have also inherited the first female's myotonia; while those who have inherited the first female's average-sized musculature, have inherited the first male's normal muscular state.

The last feature assumes somewhat greater significance when the other inherited characters are considered together with the inheritance of the two characters just spoken of. The tabulated inherited characters are as follows: the muscular condition, the size of the muscles, the colour of the eyes, hair and skin, the form of the nose, the facial expression, the mental state and the sex. It must be understood at the outset, however, that conclusions respecting the colour of the eyes and hair drawn from ordinary observation, as was done in the present instance, are not entirely reliable. The writer was assured by so eminent an authority on Mendelism as Professor T. H. Morgan that, with the exception of the colour of the skin, exact colour determinations are made possible only by means of rather complicated tests. In estimating the colour of the hair, allowances must be made for the shade, which varies with age. Nothing has been said in the report of the cases about the form of the nose and the facial expression, because these characters are even more difficult to define with any degree of exactness than is the colour of the eyes and hair.

The shape of the nose in the myotonic members of the family appears in several ways different from that in either the psychotic or the normal group. A single instance will suffice for illustration: the tip of the nose in these myotonic persons is pointed; in the three members of the psychotic group it is rounded. The four types of normal persons have as many different types of noses; Estelle's nose, for example, is of the "humped" variety, and exactly like her father's.

The expression of the face as a single hereditary entity is a good example of that conception of the Mendelian unit character which is so thoroughly condemned by Pearson [30], Conklin [7], Morgan [27], and other experts in Mendelism. A moment's thought must indeed make it plain to anybody that a great number of items, both structural and functional, conspire in the production of a given facial expression. The inheritance of that "unit character" must imply, therefore, the inheritance of all the numerous factors which constitute it.

It is the opinion of the older members of the affected family—and that opinion is largely upheld by photographs—that all the myotonic members have inherited the tip of the nose and the facial expression from the grandfather—the first male; and that the psychotic members have inherited these characteristics from the grandmother—the first female.

In the following table the particular form of the nose will be designated as pointed, rounded or humped; and the different facial expressions as A, B and C.

From this table we gather the following facts:—

(1) That with the exception of *myotonia* and *no myotonia*, the recorded characters of the first male, as well as those of the first female, formed an unbroken chain which was transmitted as a whole, constituting the general appearance and the mental state of the particular individual.

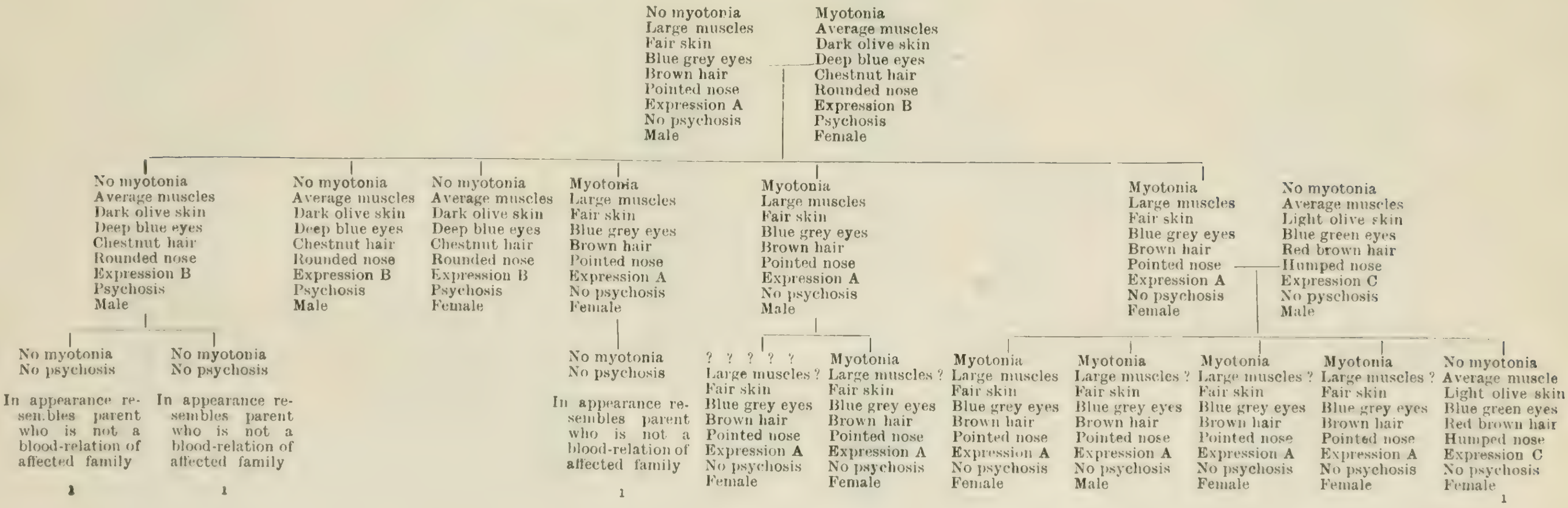
(2) That in some of the offspring the general appearance and the mental state of the first male, in others those of the first female, have proved to be dominant.

(3) That the offspring who have inherited from the first male his general appearance and his normal mental state, have also inherited from the first female the character of myotonia.

(4) That the offspring who have inherited the general appearance and the abnormal mental state of the first female, have also inherited from the first male the normal state of his musculature.

(5) That myotonia is not sex-linked in these cases.

A TABLE OF RECORDED INHERITED CHARACTERS.



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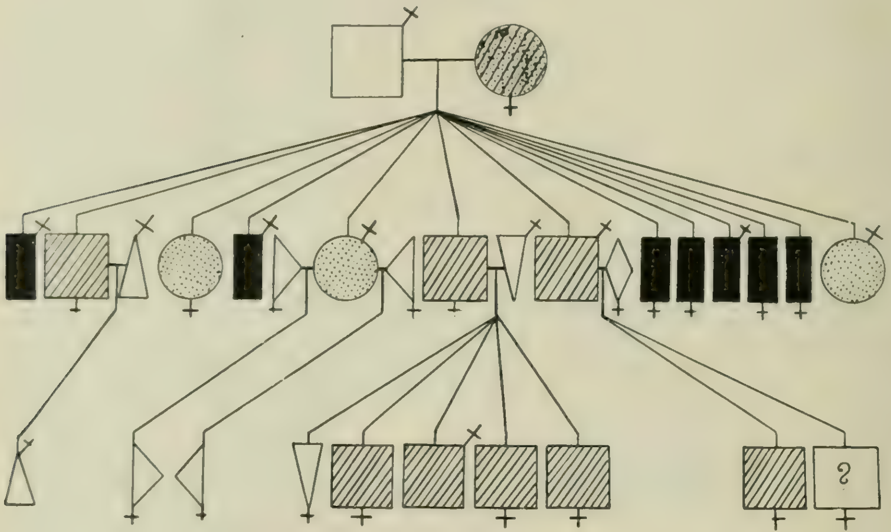
[1] An example of the four new types is that of the female at the extreme right. In appearance she is like her father (immediately above) who is not a blood-relation of the family.

The records on myotonia congenita make no mention of the association of any special physical characteristics with the muscular abnormality, with the exception of a large musculature. Since no general inference can be drawn from a single instance, we are for the present justified in the conclusion that *the particular character which offered a ready linkage to the character of myotonia, was that of a large musculature.*



□ = A large musculature and other physical characteristics of the first male.
○ = A musculature of average size and other physical characteristics of the first female.
▨ = Myotonia.
⁘ = Psychosis.
Blank = Normal.

△⋈◁▽◊ = New physical types. In each case the child resembles the parent who is not a blood-relation of the affected family.
▮ = Children who died very young. The physical type is not known.

Note.—The arrangement is in the order of birth.

FIG. 4.

In the case of the family in question, then, it would appear that some of its members have a large musculature, not because they are myotonic, but because the hereditary factor of a large musculature proved to be a favourable receptor for the hereditary factor of myotonia.

ON THE QUESTION OF PARAMYOTONIA.

Eulenberg [11], Delprat [9], v. Sölder [39], Senator [38], Martius and Hansemann (25) and others, have described cases in which a tardy relaxation of the contracted muscles occurred only in the cold. In some of the cases of the first two authors the muscles remained contracted for long periods of time, in some instances for hours. Erb [10] was of the opinion that cases of this sort belonged to an entirely different category. The affection has received the name of paramyotonia. That there is hardly any justification for setting such cases aside in a different group from Thomsen's disease will appear from the following considerations:—

Quite a number of observers point out the fact that the manifestations of Thomsen's disease are much more apparent during the prevalence of cold weather. Kron [23] goes so far as to include the influence of cold in increasing the prominence of the symptoms among the points which justify a diagnosis of myotonia. In Case 2 of the present series, the myotonic reaction of certain muscles, which was not apparent under ordinary circumstances, was demonstrated after chilling the parts. In Case 5 the myotonic condition of the musculature is exaggerated in a most striking manner in cold weather and by slight general indispositions, such as the menstrual period or an ordinary coryza.

No two of the eight cases of the present series are of the same grade of severity, nor do any two exhibit quite the same manifestations of the affection. In one the tardy relaxation of the muscles occurs only when their contraction has been brought about by a primitive form of stimulus—the so-called emotional or psychic stimuli of fright or anger—and then the myotonic phenomena are most pronounced. In another, almost any stimulus capable of evoking a muscular contraction is sufficient to manifest the myotonic condition of the muscles. In still others only stimuli applied directly over the muscle bring the abnormality to light. The fact that in some of the cases classed under the heading of paramyotonia Erb's classical reaction could not be obtained, means only that a muscular contraction brought about by a stimulus applied from outside directly over the muscle was not sufficient to elicit the myotonic reaction of that muscle. It will be remembered that in Case 8 of the present series such stimuli were ineffective, while the contraction of the orbicularis palpebrarum brought about by the act of sneezing showed beyond a doubt the myotonic condition of that muscle.

Viewing the matter from this standpoint, one is no longer surprised to find that two members of the paramyotonic family described by

Delprat were affected with typical forms of Thomsen's disease. As is the case in every other disease, the manifestations of Thomsen's disease are somewhat different in different persons, and different in the same person under varying conditions. Yet for all its variations the main feature of the disease remains the same—an inherited affection characterized by the failure of the contracted muscles to relax with a sufficient degree of despatch.

MYOTONIA WITH MYATROPHY. A MENDELIAN SUB-LETHAL FACTOR. MYOTONIA ACQUISITA.

The number of cases in which myotonia is associated with muscular atrophy is very considerable. Nearly all writers agree that the muscular strength of persons affected with Thomsen's disease, in relation to the size of their muscles, is below the normal. The coincidence of myotonia with gross muscular atrophy has been described by Hoffmann [14], Jolly [21], Schultze [37], Bettmann [4], Pelizaeus [31], Batten and Gibb [2], Nonne [29], Fuchs [13], Rossolimo [33], Lannois [24], Noguès and Sirol [28], v. Voss [42], Ramsey Hunt [16], and others. Pelz estimates the occurrence of atrophy in myotonia at 11 to 12 per cent. The fact that atrophied fibres have been found mingled among the greatly hypertrophied ones in cases where there was no gross muscular atrophy, is significant.

After observing the manner in which antagonistic muscles interfered with each other's actions, it occurred to the writer that atrophy might be caused by the repeated pulling and stretching—an actual tearing of muscle-fibres by the antagonistic muscles. The action of the facial muscles, however, would appear to be altogether too weak for such an accident to occur. Yet the facial muscles are involved in the atrophy in a great number of the cases described.

That some nerve elements are involved in the disease in a number of cases might easily be surmised from certain of the subsidiary symptoms. A number of these patients suffer with muscular pains. In the present series Cases 2, 3 and 5 complain of such pains. The diminution or the absence of some of the tendon reflexes is not infrequent in the more pronounced cases of myotonia without any atrophy, and it is very frequent in the cases with atrophy. In the most pronounced case of the present series, Case 5, most of the tendon reflexes are absent or very much diminished, yet there is no discoverable atrophy, and the muscles, when struck with the hammer, respond by normal contractions. The widespread and long-lasting paralysis caused by diphtheria in Cases 2 and 6 (at the ages of 18 and 3 respectively) compels the thought of a special susceptibility of the neural elements in these cases. Of the thirteen members of the second generation, seven died in infancy from obscure causes. Yet the family was not poverty-stricken and its manner of living not unhygienic. Although such an occurrence is not very unusual, yet the fact that the six survivors as well as their children are all affected with one chronic disease or another, naturally impels one to look for a common cause of death and disability in the stricken family.

In the light of the recent discoveries in the field of inheritance, the latter consideration should not appear as altogether far-fetched. Morgan [27] and others have described a Mendelian *lethal* factor in some of the breeds of the Chrysophila fly. In the case of the family under description we have seen that the condition of myotonia has been inherited as an independent factor from the first female; and that it has become dominant, that is to say has become manifest as a muscle abnormality, in those cases where the offspring have inherited a large musculature. But there is nothing in the history of this family, as far as it has been ascertained, to prove that the psychosis of the first female was an entirely independent factor from that of myotonia. The fact that in the records of myotonia congenita we find almost universally the muscular disorder associated immediately or mediately with psychopathies, speaks against the independence of the factor of myotonia from that of the abnormal mental state of the first female in this series. And this conjecture is rather corroborated by the fact that a certain number of the myotonics in this family, although free from psychopathy, are not free from neuropathies. After a careful consideration of the facts in connexion with this family, the suspicion has been forced upon the writer that myotonia congenita is caused primarily not by an inherited abnormality of muscular structure or function, but by an inherited sublethal factor which exerts an injurious action upon the neuro-muscular system. In seven cases the injurious action of this hypothetical agent was sufficient to determine the balance in favour of death. In other instances the existence of this agent is manifested in myotonia with atrophy of individual muscle fibrils, or of entire muscles and muscle-groups. In still others it causes myotonia, with muscular pains and a diminution of the tendon reflexes, with or without muscular atrophy. In others still, especially in cases where the musculature is not congenitally of large volume, the muscular system is spared, and the action of the inherited injurious agent is upon the highest cerebral structures.

Such a conception of the disease might help to explain not only the singular co-existence of psychoses with the muscular disorder either in different members of the same family or in the same person, but the occurrence of the temporary and acquired forms of the disease as well. If myotonia congenita is caused by an inherited abnormal content of the body fluids, then a temporary myotonia might be caused by a temporary alteration of the contents of the body fluids of a certain kind. Such a temporary alteration of the body-fluids must have occurred in the cases described by Talma [40] with an acute febrile onset and severe gastro-enteric disturbances; and by Schultze [36] in connection with gastric dilatation, associated with the symptoms and signs of tetany. The same principle might be applied to the cases where myotonia has occurred in the course of severe disturbances of the central nervous system, such as the case of brain tumour described by Bremer and Carson [5]; of myotonia associated with athetosis described by Kaiser [22], and of myotonia occurring in connection with syringomyelia, mentioned by v. Frankl-Hochwart [12] and by Schlessinger [35].

A Psychological Concomitant of Thomsen's Disease.

It will appear from the history taken in connection with Case 2 that the myotonic mother of four myotonic children, and herself the daughter of a myotonic mother, was reluctant to admit that she suffered from any muscular disorder. As a matter of fact she strenuously denied the existence of the disorder in any member of her family, and this denial was maintained for weeks in the face of numerous facts to the contrary.

Such an attitude of mind appears to be a pretty constant concomitant of the muscular disorder, and is mentioned by a number of writers. Jendrassik [19], in his able summary of the affection, mentions the fact that "the patients seek to conceal their infirmity by all sorts of artifices." Thomsen himself must have been thoroughly aware of this attitude in his own case when he said: "There is an active psychic factor involved, namely, the fear of ridicule. As soon as the feeling arrives that those about will discern and observe the disability, the symptoms become aggravated in the highest degree." In the present case of the mother of the myotonic children there was, in addition to the desire to conceal a lifelong disability that is so thoroughly disguised by an appearance of perfect health and strength, another inhibitory factor. It was the wish to suppress the consciousness of a responsibility of having transmitted her infirmity to future generations, innocent as she certainly was of any wrong motive at the time when the responsibility was taken.

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A CONTRIBUTION TO THE ANATOMY OF SPINA BIFIDA.

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INTRODUCTION.

THE purpose of this paper is to emphasize certain features in the minute structure of cases of spina bifida which have a direct bearing on details of operative procedure, and on prognosis as regards nervous function after and apart from operation.

Recent medical literature contains few accurate descriptions of specific cases of rachischisis, and the discussion and diagrams in the average surgical treatise are imperfect in detail and often misleading. Since Virchow, Lebedeff and v. Recklinghausen in the eighties, first called attention to the embryological basis of the defect, very little new work has been done, and it appears that this early work has been largely lost sight of. Surgeons have depended upon operative findings which are necessarily incomplete, and pathologists have left these deformities severely alone. It is true that the study of anomalies in many instances is not a fruitful one. To the study of this particular group of abnormalities, however, much practical value attaches, as a large proportion of the less severe types demand surgical relief. The number of cases here reported is small, and the records in some are necessarily incomplete, but material of this nature is difficult to obtain, and especially so in the milder cases round which surgical interest centres.

Before passing to the discussion of individual cases it seems advisable to recall briefly the normal development of the structures which are defective, and the general morphology of the types of defect encountered.

Development of Central Nervous System and Vertebral Column.

The central nervous system first appears as a thickening of the surface ectoderm along the mid-dorsal line of the embryo, the medullary plate (fig. 1, A). The edges of this plate rise, turn toward the mid-line and finally meet and fuse, forming a closed tube (fig. 1, B, C). Fusion is segmental in character; it takes place first in the cervical region, and

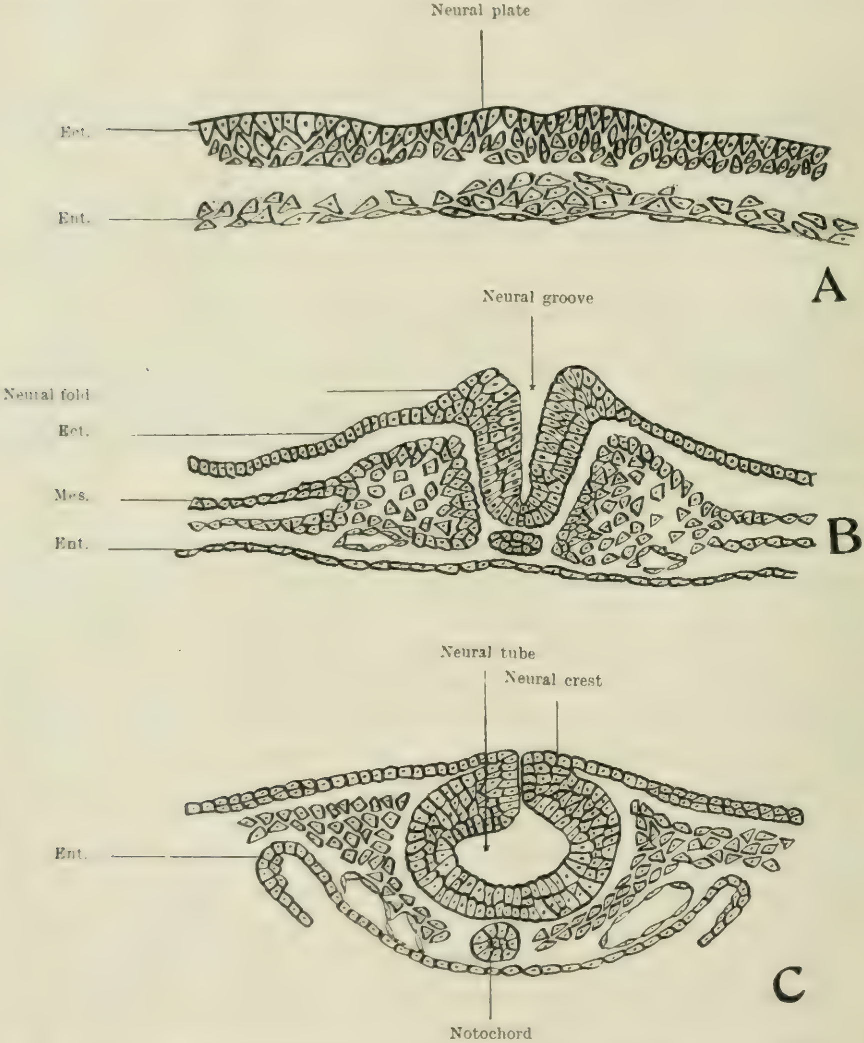

FIG. 1, A, B, C.—Transverse sections of chick embryos, showing stages in the formation of the neural tube.

progresses backward and forward, being delayed longest in the cephalic and caudal segments (fig. 3). Ultimately the closed neural tube sinks beneath the surface, mesodermal structures interpose themselves and the neural ectoderm continues its growth independently of the integument. In the regions last closed there remain for some time minute openings, the neuropore at the anterior extremity and the caudopore at the posterior, through which the central canal communicates with the exterior. Ultimately these openings also become closed.

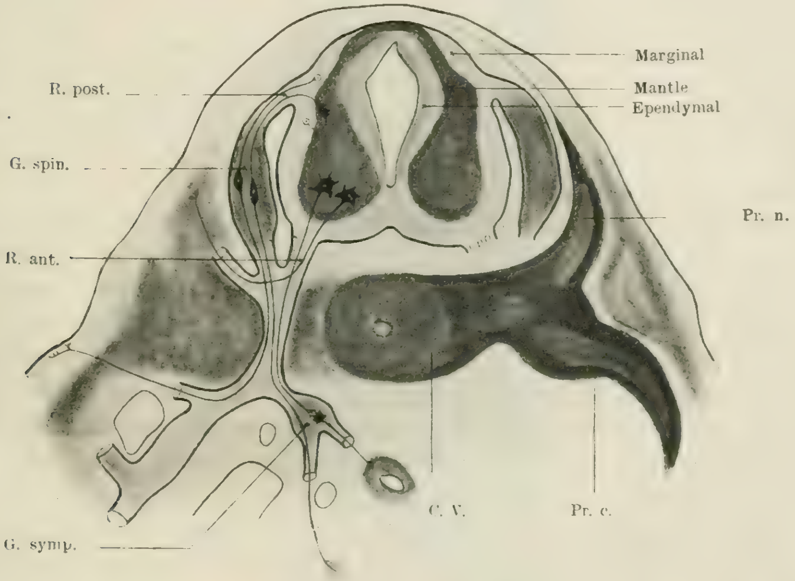

FIG. 2.—Schematic. Left side modified from *Prentiss and Arey*, showing the origin of the spinal ganglia and the spinal nerve roots. Right side represented as though sectioned through vertebral body, showing the early stage of vertebral development with the origin of the neural arch.

In the meantime, even before the medullary folds have completely fused, an increase in size of the cephalic portion of the folds becomes apparent and one can differentiate the brain from the spinal cord (fig. 3). It is not necessary here to deal with the complex further development of the cerebral vesicles, but attention must be confined to that of the cord. In its separation from the surface ectoderm there persists for a time at the mid-line a chain of cells, the neural crest (fig. 1, C), having the characteristics of the cells of the neural tube proper. From this chain are formed the posterior root ganglia (fig. 2, *G. spin.*) and the ganglia of the sympathetic system (fig. 2, *G. symp.*), as well as the nerve cells found in various viscera.

The further development of the spinal portion of the neural tube consists in the rapid proliferation and specialization of its cells resulting in a differentiation into three zones, outer, middle and inner, distinguished by the grouping and ultimate fate of their cell contents. Certain of the cells become neuroblasts, the forerunners of neurons; certain others, also ectodermal, become supporting glial cells. The inner zone (fig. 2, *Ependymal*) undergoes but little increase; it consists of glial cells only, which form the ependymal lining of the small persistent central canal and the narrow surrounding layer of gelatinous tissue. The middle zone (fig. 2, *Mantle*), containing the neuroblasts, becomes the grey matter of the cord; the outer zone (fig. 2, *Marginal*) becomes the white matter, consisting of the processes from the neuroblasts of the middle zone and of the spinal ganglia, supported in a meshwork of neuroglia.

The middle zone rather early becomes differentiated into an alar, posterior lamina, and a basal, anterior lamina. In the alar lamina are developed the structures of the posterior horn. In the basal lamina are developed the motor nerve-cells of the anterior horn, and the emerging fibres of these pass out as the anterior nerve roots (fig. 2, *R. ant.*) between the segments of the developing vertebræ. Meantime the spinal ganglia which have formed from the neural crest pass ventrally and laterally until they lie in the spaces between the vertebræ, in close contact with the anterior nerve root fibres. From the cells of the ganglia processes pass into the outer zone of the cord and form the posterior roots (fig. 2, *R. post.*) of the spinal nerves. Fibres from these ascend in the posterior columns; others form synapses about the cells of the posterior horn. These relations are shown diagrammatically in the left side of fig. 2, representing a cross section of a 10-mm. human embryo.

While these changes are occurring within the neural tube, mesendermal structures come into relation with it, and form a delicate sheath, which later becomes separated into three layers, pia, arachnoid, and dura mater. Anteriorly, the vertebral column is developing with the notochord, which is shown in fig. 1, A and B, as its point of departure.

The right half of fig. 2 shows diagrammatically an early stage in vertebral development. Surrounding the notochord is the rudiment of the body of the vertebra (*C. V.*), with the beginning of a costal process (*Pr. c.*) and a second process (*Pr. n.*) directed dorsalward and partly enclosing the spinal medulla. This is the neural process from which develop the laminæ and the spinous processes. The laminar processes grow out from the neural process toward the mid-line of the embryo, surrounding the spinal cord and forming the spinal canal. In a fœtus of 33 mm., about nine weeks, they extend well out towards the mid-dorsal line, and are united across this by a membrane of connective tissue. In one of 50 mm., about the eleventh week, they are united so as to form a canal similar to the adult spinal canal, and small spinous

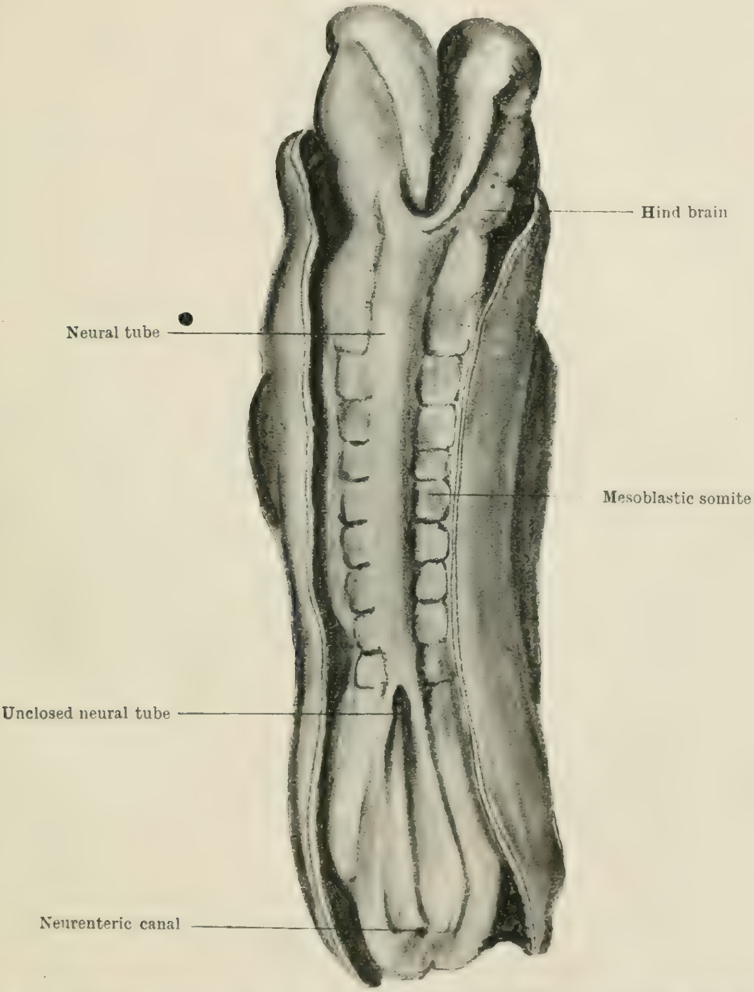

FIG. 3.—Human embryo of 2·11 mm., showing closure of neural tube, and early stage in differentiation of cerebral region. (After Keibell and Mall.)

processes are developed upon them. The completion of the spinal canal takes place earlier in the thoracic than in the cervical and lumbar regions.

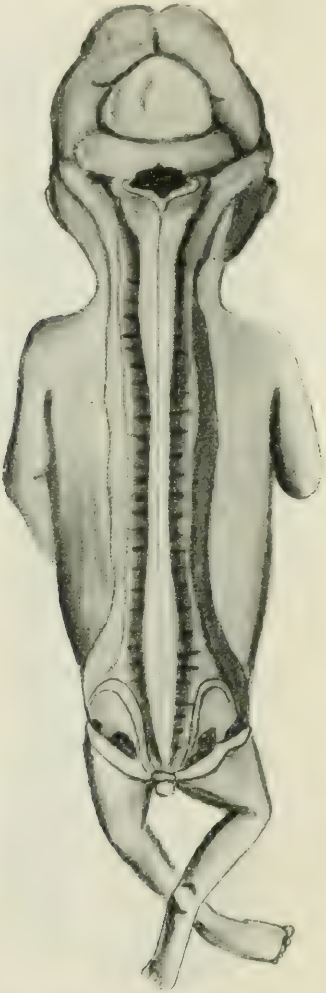

FIG. 4.—Human embryo, aged 3 months, showing the spinal cord extending to tip of coccyx. (After Keibell and Mall.)

During this period, as is shown in fig. 4, the cord extends throughout the whole length of the spinal canal, and the nerve roots and spinal ganglia formed in each segment take up a position between the bases of the neural arches, in the future position of the intervertebral foramina. Growth of the neural tube and of the vertebræ progresses at equal rate until the third month, and up to this time the nerve roots continue to pass out of the canal perpendicularly to the long axis of the cord. Fig. 5, A, shows a diagrammatic representation of the relative positions of neural and of vertebral segments at this stage. In the further growth of the embryo, however, the growth of the neural tube is outstripped by that of the vertebral column, and as it is anchored above by its attachment to the medulla it remains high in the canal, terminating at birth at the level of the third lumbar vertebra (fig. 5, B). This is usually referred to as "the upward migration of the cord." At the tip of the coccyx, the extremity of the cord remains for a long time connected with the surface (fig. 5, A), and this connection pulls the end of the cord and the pial sheath into the slender filum terminale (fig. 5, B). It will be necessary to describe this in greater detail later, as it has direct bearing on the defects which occur at this region of the neural canal. The spinal nerves, having a fixed relation to the intervertebral foramina, are carried away from the cord segments with which they are connected by the growth of the vertebræ. Their roots elongate to compensate for the unequal growth, so that while those from the upper segments continue to pass out almost horizontally, those from the lower segments descend more and more within the canal as one passes downwards. At birth a cauda equina is found similar to that in the adult. Fig. 5, B, shows schematically the relation of cord, spinal ganglia and nerve roots as they are found in the full-term fœtus; it does not differ materially from that in the adult. It should be mentioned that in making fig. 5 the skeletal basis of the diagram was drawn to scale from an actual dissection in a seven months' fœtus. For purposes of comparison this skeletal scheme was used for all the diagrams in this figure, as the particular change under consideration seemed better brought out in this way.

The formation of the filum terminale and its relation to the coccygeal segments of the cord has a direct bearing on the structure of lumbosacral spina bifida as it differs from spina bifida in other areas of the neural tube, and must therefore be discussed in slightly greater detail. The coccygeal segments, with the exception of the first, are rudimentary. Their cells do not differentiate beyond the embryonic stage of a layer of glia cells surrounding a central canal. The last coccygeal segment remains attached to the surface ectoderm, and with the increased growth of the vertebræ this undifferentiated area becomes drawn out into a slender thread of glia in which for a long time there

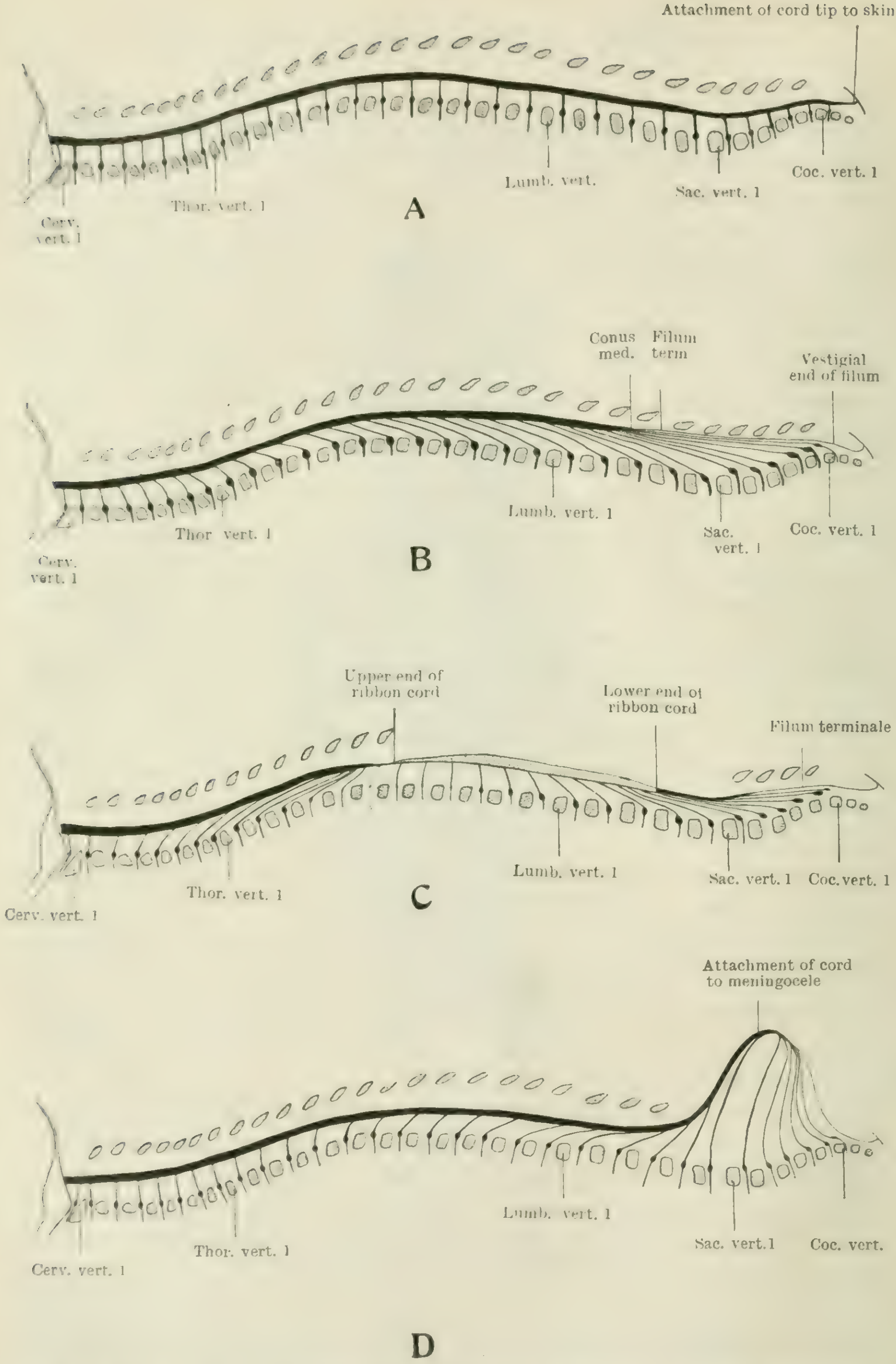

FIG. 5, A, B, C, D.—Diagrammatic representation of migration of cord and relations of nerve roots: A, in 3 months' fœtus; B, in fœtus at term; C, in Case I, myelocele; D, in Case III, myelomeningocele. The skeletal basis of all the figures was taken from a dissection of the spinal column of a 7 months' fœtus.

is a persistent central canal. It remains attached to skin by its tip, and higher up in the rudimentary coccygeal part of the spinal canal it is separated from the skin only by imperfectly differentiated meningeal layers, and by a band of fibrous tissue which alone represents the vestigial coccygeal laminæ (fig. 5, B). Even in the full-term fœtus nervous elements can still be found in it. The filum terminale as low down as it remains glial represents, therefore, the lower four coccygeal (tail) segments, which have become drawn out so that they stretch from the tip of the coccyx to the level of the first coccygeal cord segment which lies at the level of the third lumbar vertebra. The normal adherence of the end of the cord to the skin surface, and its persistent rudimentary state in this region, have a direct effect in producing one variety of meningomyelocele found in this region of the spine.

Morphological Basis of Spina Bifida.

It is not within the scope of this paper to enter into the underlying causes, probably of a bio-chemical nature, which determine the occurrence of spina bifida and of other basic developmental defects. It is necessary merely to point out the morphological factors which are concerned in this particular class of cases.

Apparently the mechanism of closure of the medullary folds is one of the most delicately adjusted of developmental processes, for anomalies are of fairly frequent occurrence both in man and in other vertebrates. In chick embryos which have been improperly incubated it is a common experience of the embryologist to find a number in which the folds have partly or entirely failed to unite in the usual time sequence with other organs. Usually very young embryos only present this deformity, probably because the older individuals die from the unfavourable conditions which have produced the defect. Other laboratory embryos, as opossums, pigs, &c., present the defect more rarely, doubtless because of the normal conditions of their existence, as these embryos are fixed and prepared in utero, and not artificially incubated.

It will be seen that any interference with the closure of the medullary folds will, of itself, cause a corresponding interference with the development of the neural arch of the vertebra forming around that region of the cord. Any defect, however slight, involving the medullary tube proper, is associated with defect of the vertebral neural canal. Such medullary tube defect has morphologically a wide range of possibilities, from mere delay in the closure of the caudopore with a consequent delay in the development of the membranes of the cord in this region and of the integument covering them, to a complete lack of the infolding of the medullary plates, with or without differentiation of the neural ectoderm forming the plates. In certain cases the defect in the medullary tube has been so slight or so evanescent that in the fully developed embryo no trace of defect remains in the cord itself, but its existence is revealed by an imperfection of membranes associated with a corresponding defect in the vertebral canal. In still other cases, one finds no such definite evidence of an original medullary tube defect, the anomaly consisting merely of a failure in the fusion of the vertebral spines or of the laminæ. More rarely laminæ are partly or wholly absent. This is probably also dependent in a proportion of cases on medullary tube defect, for nervous symptoms are not infrequent. Reference will be made to this later in the discussion of the types of spina bifida encountered in actual specimens.

It will be seen that all these variations of the deformity may occur throughout the entire length of the medullary tube, or may be limited in extent. The development of the cephalic extremity of the tube and of the cranium is so divergent from that of the spinal cord that no attempt will be made in this paper to discuss defects involving the brain (cranio-rachischisis). It must be remembered, however, that defective development of one part of the neural tube is prone to be associated with defective formation of other parts, and cephalic abnormalities are frequently found with spinal. Fusion of the spinal part of the medullary folds tends to be normally later in the cephalic and in the caudal ends of the embryo than in the mid-thoracic regions, and local defects are more apt to occur at these points; but the fusion is segmental in character and segments at any region may fail to unite without necessarily impeding the union of segments above or below. The rudimentary character and morphological peculiarities of the coccygeal segments (filum terminale) already alluded to may be responsible for the great number of defects occurring in this region.

It is particularly necessary to remember the time sequence of the structures which participate in the defect. Normally the entire neural tube is closed at the end of the third week; it is then the full length of the embryo. Normally the vertebral neural arches from the first cervical to the third or fourth sacral are closed at 50 mm. (eleventh week); the arches below the fourth sacral are normally rudimentary. The defect, whether it be a failure of closure of the medullary groove, or an adherence of meningeal layers to skin, cannot occur after the vertebral arches are closed; and at this period of growth and indeed for a short time thereafter (third month), the vertebral column and the spinal cord are increasing in size *pari passu*, so that each cord segment lies in line with the corresponding vertebral segment. However, should defect occur, the general development of the remainder of the embryo may go on unaltered except by mere mechanical hindrance at the point of defect. It is also possible that growth in size and histological changes may occur even in the defective area, as though it were morphologically perfect. On the other hand, if the morphological defect is great, or has been produced at a more "critical period" in the development, no growth nor differentiation of tissues may occur, and in such cases the mechanical factor determining other local changes may be greatly increased.

It is necessary to emphasize these points because it has been customary to describe rachischisis as though the parts involved bore the same relations to their surroundings at the time of the origin of the defect as they would normally bear in the same locality in the fully developed fœtus.

TYPES OF SPINA BIFIDA.

If the entire length of the spinal canal remains open the condition is known as *rachischisis totalis;* if a considerable number of segments are involved, but not all, it is known as *rachischisis partialis;* if a small number are involved,. the remainder being normal, *rachischisis restricta.* If the neural groove has remained open the rachischisis is said to be *complete;* if it has closed, it is *incomplete.* Rachischisis totalis is practically always complete in its entire extent, but there appear to be a few cases in which the lower segments of the cord have closed and are covered by meningeal layers, though skin and vertebræ are defective. In rachischisis partialis part of the defect is complete, but in practically all cases part will be found to be incomplete. In rachischisis restricta the majority of cases are incomplete, a few complete, and a considerable number are incomplete in some of the segments and complete in others. The further classification is rendered difficult by the merging of one type into the other due to the varying degrees of causative defect; it is perhaps most satisfactory if it is made upon an embryological basis.

The varieties fall into three classes from an embryological point of view: (1) Those in which the gross defect is limited to mesoblastic structures. (2) Those in which the defect is mainly mesoblastic, but in which there is a slight ectodermal defect. (3) Those in which the gross defect is ectodermal and the mesoblastic condition is a mere accompaniment. Probably in the more severe cases of Class 1, and in all cases of Class 2, the causative factor is primarily ectodermal, but the imperfection of this has been obscured by its relatively normal aftergrowth.

Class 1.—Mesoblastic defect (rachischisis incompleta restricta).

(A) *Spina Bifida Occulta.*

The simplest forms of this type are those in which the spines of one or more vertebræ are bifid either at their tips or to the bases of the spines. The spines of the upper cervical vertebræ are normally bifid in Europeans, but one frequently finds in the dissecting room a seventh cervical with bifid spine, and more rarely other vertebræ. These cases never give rise to symptoms, and are probably never associated with nervous defect.

A more serious anomaly is that in which the laminæ (neural arches) are incompletely formed or entirely lacking. In the normal spinal column the fourth sacral sometimes, and the fifth sacral and coccygeal vertebræ always, present this defect, and it is not infrequently encountered in the higher sacral and the lower lumbar vertebræ, without any associated lesion of meninges or cord. More rarely the absence or imperfection of the laminæ is accompanied by an adhesion between meninges and integument, abnormal fat development, or peculiarities of the epidermal structures, as hypertrichosis. Without such external evidence of anomaly the condition is not ordinarily discovered except in the course of a chance X-ray examination, or of anatomical dissection. In a certain proportion of cases, however, the adhesions or the overgrowth of fatty tissue cause pressure symptoms, and anæsthesia, paræsthesia, or paresis call the surgeon's attention to the condition, and operation for the relief of pressure reveals the true nature of affairs. A certain number of these cases probably represent small meningoceles of Class 1 (B) which have become obliterated in early life.

(B) *Meningocele.*

Here the vertebræ are defective, and in addition there is present a cystic protrusion of the meninges. Careful examination of cases of this type shows that the relationship of the various meningeal layers presents wide variations. In some differentiation of the integument has proceeded normally, and the cystic tumour is covered by well-formed skin. In the majority, however, the integument is thin, covered by imperfect epidermis and adherent to the presenting meninges. To this imperfect skin the term "parchment" is fittingly applied; it is poorly vascularized and of low vitality. On opening into the sac and examining its walls one may find a variety of conditions. (1) The sac wall may be composed of fused dura and arachnoid, or of these two layers in close proximity but not fused, forming a distended single sac representing the subarachnoid space, in the bottom of which the cord courses down covered by pia in the normal manner. (2) The dura and the arachnoid may be separated by a collection of fluid, the tumour consisting of an outer dural and an inner arachnoid sac, the pia and cord being normal. (3) The outer layer of pia may be likewise distended, forming a third, usually much smaller sac, within which the cord lies. (4) In any one of these forms the cord may be lifted up by the fluid round it, and may course through the middle of the cyst, presenting, however, no obvious abnormality. This condition, however, does not seem to be well authenticated.

Class 2.—Mesoblastic defect with slight epiblastic defect: (rachischisis incompleta restricta).

(*A*) *Myelo-meningocele.*

Here we find a meningocele in which the neural tube has closed but has remained in contact with the surface ectoderm in a small part of its extent, the result of delayed closure usually near the caudopore. The cord is drawn by adhesions to the surface of the sac, and is attached by a greater or less portion of its length to the sac wall. The nerve roots may pass down from its ventral surface to reach their foramina, or may be caught in the adhesions and course down over the surface of the sac. These cases are always covered by parchment skin, but by the microscope integumentary structures may be demonstrated lying dorsal to the neural tube. This variety is probably confined to lumbosacral rachischisis, and is the result of the peculiarity of the development of the coccygeal segments already noted; it is, however, often confused with more severe types in which some cord segments have not closed, and many cases described in this class more properly belong to Class 3 (A).

(*B*) *Hydro-myelo-meningocele.*

In certain cases in which the neural tube has closed, either with or without a persistent adherence to the surface ectoderm, as was described above, the central canal of the cord becomes enormously distended by fluid, and within a meningeal sac of any of these types a medullary sac may be found, the wall of which is formed of thinned nervous tissue, from which more or less perfect nerve roots pass. This form is not infrequently encountered, and is entitled to separate mention because of the importance of differentiating it from the pure meningocele which it resembles clinically. It represents only an exaggerated form of the concomitant hydro- and syringo-myelia which are so frequent in the more severe grades of rachischisis.

Class 3.—Gross epiblastic defect with accompanying mesoblastic defect (rachischisis completa).

(*A*) *Myelocele* (*Rachischisis Completa Restricta*).

Here two or three segments of the medullary folds have remained open and the neural ectoderm lies exposed on the surface of the body as a ribbon of delicate tissue down the mid-dorsal line. On either side the meninges are attached to the edges of the medullary ribbon, and form a zone of parchment skin which passes in turn into normal skin. In certain cases no collection of fluid occurs, but in the majority the meningeal layers become filled with fluid as in pure meningoceles, and the open neural ribbon is stretched over the surface of a tense sac. Cases of this type occur in the cervical region, very rarely in the thoracic, but often in the lumbo-sacral region. In the cervical and thoracic regions they are easily differentiated, but in the lumbo-sacral they are apt to be obscured by the growth of surface ectoderm over the lower part of the neural ribbon. The lower coccygeal segments, functionless in man, never develop beyond the simple neural tube of the embryonic state. The last coccygeal segment normally remains attached to the skin. The tendency of all these segments is towards atrophy rather than growth, while the growth of skin ectoderm is as active as elsewhere in the body. If the upper coccygeal segments do not close, the few neural cells present in them tend to become atrophic and overgrown by skin, and this part of the neural tube is prevented from elongating into the filum terminale. The adhesions to skin so formed mechanically drag down the sacral segments and involve them in the defect. In the lumbo-sacral variety also, probably as a result of the adhesions to skin, fluid is especially apt to collect in large quantity, and its pressure within the meningeal sac may be so great as to draw the normal cord above the open segments down out of its canal and into the sac. Thus a normal cord may appear to end in the middle of the sac wall, and the open medullary groove segments below may be covered by inflammatory exudate or by overgrown integument so that the significance of cord attachment is entirely overlooked. Careful study will probably result in placing many of the cases which have formerly been placed in Class 2 (A)—rachischisis incompleta—in this class with other complete defects.

With these, as in other cases of cord involvement, hydromyelia and syringomyelia are often associated.

It is customary to refer to the cases of this type in which the meninges are filled with fluid as cystic myeloceles, but while this term has some descriptive value it does not denote any class distinction.

(*B*) *Myelocele* (*Rachischisis Completa Partialis or Totalis*).

These cases do not differ from those in Class 3 (A), except in the extent of the defect, which involves a very large number or all of the neural segments. Because of the extent of the defect there is never an accumulation of fluid in the severer cases. The neural tube lies flattened out in the groove formed by the undeveloped vertebral laminæ upon the surface of the exposed vertebral bodies. The meningeal layers are developed beneath it and pass laterally into a zone of parchment skin which blends with the normal skin. In the cases of total defect, where there has been no abnormal adherence of the cord to the skin over the coccyx, the ribbon cord may migrate upward as in the normally developed cord, and here the lower sacral vertebræ may continue their development, without interference by the neural defect. Total neural lesion may therefore occur without total vertebral defect. This is important because of its bearing on the problems presented by the restricted lesions of the same class.

In both the types just mentioned the medullary tissue may present wide variations in the extent to which the differentiation of its cells has occurred. In some instances the condition remains embryonic, and no trace of the adult medullary structures is to be found ; in others the cord substance has developed as though closure of the folds had been accomplished, and the nerve cells and roots can be easily distinguished.

Statistics of the percentage occurrence of spina bifida in its various manifestations are difficult to collect. From observation in the anatomical laboratory it appears that mere vertebral defect is of fairly frequent occurrence. Various forms of meningocele come frequently to the attention of the surgeon, but are infrequently reported, so that no accurate idea of their frequency can be formed. The cases with marked medullary involvement are often born dead, or succumb shortly to infection. As they are not remediable, they attract but little interest on the part of the obstetrician.

Surgical interest centres about the cases of spina bifida restricta, since it is in these cases that operative interference is feasible. Here, however, while more case records are available, their imperfect nature and the varied use of descriptive nomenclature makes accurate classification a matter of extreme difficulty. This is especially true of those of Class 2, in which there is involvement of the cord.

Before going further it will be advisable to discuss the few cases here studied in detail, and to point out the difficulties of recognizing the types from operation or gross dissections only.

Discussion of Cases.

Method of preparation and study of specimen.—The material studied is partly operative and partly pathological museum specimens. The conditions under which it was obtained made certain features of the accurate study difficult. In the three operative cases (Cases III, IV, VII) it was the writer's good fortune to assist at the operation and in the care of the patients, so that the observations on these were carried out as a continuous first-hand study. In each case drawings were made from the actual specimens, enlarged to scale, and wherever any matter of personal interpretation of the condition modifies the diagrams it is clearly indicated in the description. It will be obvious that certain features of a preserved specimen can be brought out only by personal observation.

In making the microscopic study of the specimens, blocks of tissue of 2 to 3 mm. thickness were cut, embedded in celloidin, and stained by the following methods: (1) toluidin blue; (2) iron hæmatoxylin; (3) hæmatoxylin-eosin. In one or two cases other methods were tried, but as they were not fruitful they were abandoned. All the sections from each block were stained and examined, and the interpretation of certain features in the individual sections was frequently the result of this study. In certain cases where the condition was obscure additional sections were made above and below the original blocks, but detailed description of these is not given. The sections photographed and described are those which appear to throw most light on the anatomical and clinical aspects of the cases. All the photographs were made with a $\frac{3}{4}$ in. objective and reduced to the same scale, so that comparison of their size could be made. They were re-touched with indian ink with constant reference to the slide from which they were made, in order to indicate myelination and nerve cells.

CASE I.

Myelocele—spina bifida completa partialis, of Class 3 (B). Specimen No. 1109, Surgical Pathology Museum.

The specimen was received as part of a pathological collection which came into the department of Surgical Pathology of the University of Texas, and no history could be obtained. The preservation was not all that could be desired, and no care had been taken to protect the myelocele from injury in transportation. The body was in good condition, however, except for the more delicate neurological examinations of the brain. The body was that of a negro female fœtus, length 24 cm. from vertex to coccyx. External appearance is shown in fig. 6. Limbs and trunk were well developed in form and musculature. External genitalia and anus normal. Head is hydrocephalic, circumference 41 cm. (occipito-frontal). Face and oral cavity normal. Spina bifida completa extends from level of eighth thoracic vertebra to that of the upper margin of sacrum.

Dissection.—On opening the ventral body wall a diaphragmatic hernia is seen, the greater part of the abdominal contents occupying the left thoracic cavity. The right side of diaphragm is normally developed; the left side presents a widely open pleuro-peritoneal hiatus, through which the whole of the stomach, small intestine, appendix, the first part of colon, spleen, and left lobe of liver protrude into left chest. The heart and pericardium are normal except that they are pushed to the right of the mid-line by the herniated viscera. Right lung is normal in shape, atelectatic, smaller than normal on account of pressure: left lung is very small, about one-fourth normal size and flattened. Thymus is displaced toward the right, but otherwise normal. Examination of the abdomen shows it to be occupied by the right lobe of liver, which is normal except for a distortion in shape due to the herniation of its left lobe and to the abnormal position of the other viscera, and by the descending colon and a large convoluted sigmoid, which occupy their normal positions. The adrenals and the genito-urinary system are normal.

Microscopic examination of the organs was not made, as they gave no sign of structural abnormality.

Skeleton.—Maceration for slight anomalies was not done because of the desire to keep the specimen for demonstration purposes. So far as could be determined without maceration, the skeletal system is normal excepting that the calvaria is typically hydrocephalic, its sutures very wide, and the bones thin and soft. The base of skull and the cervical and upper seven dorsal vertebræ are normal. The lower five dorsal and all the lumbar vertebræ present large flaring laminæ which are curved with the convexity anterior, so as to present on the dorsal surface a wide shallow ditch. The prominences of these laminæ are clearly distinguishable beneath the thin parchment skin of the region (fig. 7). Ossification centres are normal in site and size, in the bodies and laminæ. The sacrum is normal.

Nervous system.—Accurate examination of the brain was impossible because

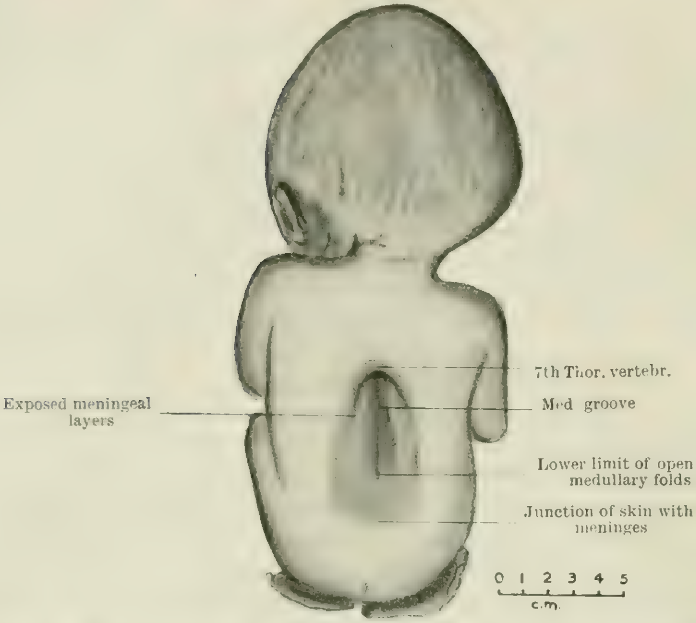

FIG. 6.—Case I, myelocele. External appearance of specimen before dissection.

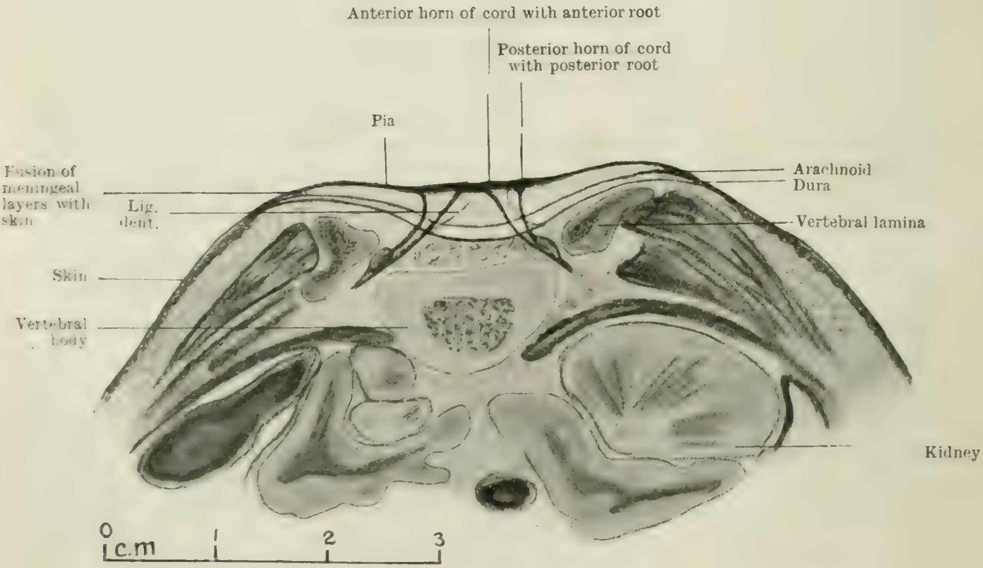
Anterior horn of cord with anterior root
Posterior horn of cord with posterior root
Pia
Fusion of meningeal layers with skin
Lig. dent.
Arachnoid
Dura
Vertebral lamina
Skin
Vertebral body
Kidney
0
c.m
1
2
3

FIG. 7.—Case I, myelocele. Cross section through region of twelfth thoracic segments of the cord.

of the imperfect preservation of this portion of the central nervous system. The lateral ventricles are greatly distended with fluid and the cerebral cortex is thinned to a layer varying from 4 or 5 mm. to the thinness of tissue paper. The choroid plexuses of the lateral ventricles are large, but present no other apparent abnormality. The cerebellum is poorly preserved and appears to be represented by a mass of loose hæmorrhagic and very vascular connective tissue, with a small amount of nervous tissue at its base, apparently representing the peduncles. The mesencephalon, pons and medulla are macroscopically normal.

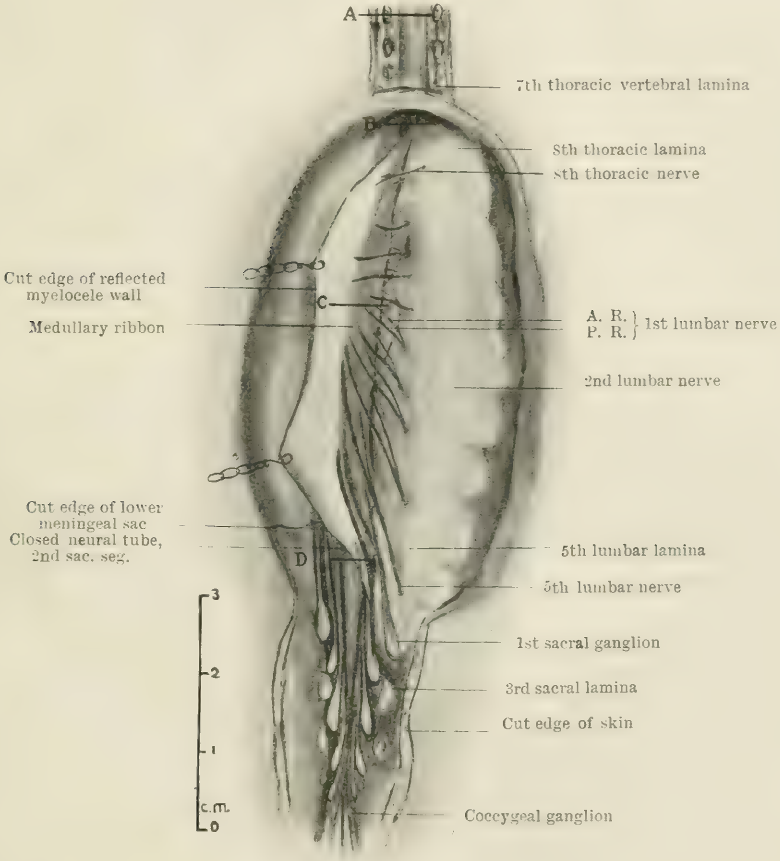

FIG. 8.—Case I. Dissection of myelocele, by reflection of lateral wall and opening the spinal canal above and below the lesion. Levels of the microscopical sections indicated by letters A, B, C, D.

The spinal canal was opened from the foramen magnum to the level of the seventh thoracic vertebra, i.e., the last normal vertebra. The meninges in this region are normal. On exposing the cord it is found to be superficially normal from the medulla oblongata to the level of the sixth thoracic vertebra; but the portion lying on the body of the seventh thoracic vertebra is small, soft and membranous, and terminates by passing under the seventh neural arch to blend with the myelocele below.

The arrangement of the nerve-roots from this whole region of cord is peculiar. The first two cervical pairs pass out almost horizontally; those below incline more and more *upward* in the canal, as is shown diagrammatically in fig. 5. C, so that the roots which pass through the first thoracic foramina come from the cord which lies in relation to the fifth thoracic vertebra. All the roots to this level are large and apparently normal except for their upward direction. At the level of the sixth thoracic vertebra the roots are very delicate, and it is not possible to trace them all, but attenuated fibres from this region appear to enter the second, third, fourth, and fifth foramina (fig. 5, C). From the membranous portion of cord lying on the seventh thoracic vertebra delicate strands pass to the sixth foramina, and possibly also to the seventh, though these may arise from the open cord below.

It is necessary here again to direct attention to figs. 5, A and B, illustrating the normal upward migration of the cord in the spinal canal. In this specimen the seventh thoracic segment of the cord was prevented from moving upward by adherence to the myelocele below. This portion of cord, therefore, represents the segment of neural tube infolded in this body segment of the embryo, and its roots pass out horizontally as they were originally laid down. They are attenuated because the normal development was hindered by the adhesions and by traction, as the length of the spinal canal above them increased. Similarly the upper cervical segments maintained their normal relationships by virtue of their attachment to the brain stem, and their roots pass out horizontally as is usual. If all the medullary tube had developed equally between these two fixed points, the preponderant growth of the vertebral canal should have resulted in an equal stretching of the whole length of the cord, the nerve-roots continuing to pass out horizontally. We find, however, that the lower portion of cord is membranous, and its small nerve-roots show that it has fallen far short of attaining its normal growth; moreover, being largely composed of connective tissue (membrane), it has apparently been much less easily stretched than the higher portions, and has remained almost stationary while the better developed higher segments have been pulled down to its level. A greater descent of the lower cervical segments would be expected, but the inequality of growth of the cervical vertebræ and cervical cord in this specimen is less than the inequality in the thoracic region.

As will be seen later in the description of the myelocele, the nerve-roots below the level of the eighth segment of the cord are also affected by the fixed relations of this cord segment to its vertebral segment, but as the caudal extremity of the cord is not fixed, the cord migration is all upward, and the nerve-roots are carried downward to their foramina, though not to such a great extent as in a normal canal. (See fig. 5, C.)

Myelocele.—In reading the description of the myelocele, it is necessary that constant reference be made to the accompanying diagrams. These were made from the actual specimen and dissections: fig. 6 was drawn life-size and reduced, fig. 7 and fig. 8 enlarged to scale and reduced.

Dissection of the myelocele.—The arch of the seventh thoracic vertebra and the tissues and skin covering it are, as already mentioned, normal in character. At the lower border of this arch, however, as shown in fig. 6, the skin dips down over it and becomes merged in the parchment skin of the myelocele. From the level of the eighth thoracic to the upper margin of the first sacral vertebra lies a translucent membrane of parchment skin, which merges below and laterally at a distance of 10 mm. from the mid-line, into normal skin. Down the middle of this (fig. 6, *Med. groove*) lies a ribbon of soft friable tissue, which passes above into the neural canal of the seventh thoracic vertebra where it is continued into the spinal cord. Below, at the level of the fourth lumbar vertebra, it sinks under the glistening parchment, and passes beneath to enter the spinal canal in the sacrum. This velvety ribbon represents the open medullary tube, and its structure will be examined more carefully later.

On cutting through the parchment near its junction with skin laterally, it is found to be composed of an inseparable fusion of the three meningeal layers of the myelocele with the integument. The epithelium of the integument is here very thin, but presents its normal stratification. Passing toward the mid-line a point is reached where the parchment can be separated into its component layers, and at this point all trace of epithelial covering is lost. The relations of the meningeal layers can best be seen in a cross-section through the middle of the myelocele shown in fig. 7. The most superficial of these layers, viz., the pia, is found to be attached to the medullary ribbon. Anterior to this is a definite arachnoid, and still deeper a thick dura. These are in close contact and are joined by delicate adhesions, which become closer as the lateral edge of the parchment is reached. The line of fusion of the three meningeal layers with skin corresponds closely with the outermost edges of the exposed vertebral laminæ. When an incision is made medial to this line of fusion and the pia is reflected, the medullary ribbon is lifted with it, revealing the condition shown in fig. 8. Posterior nerve-roots are seen to emerge from the lateral edge of the ribbon, and anterior roots more medially. Between the radicles the denticulations of the ligamentum denticulatum pass from the pia to the dura; but a few of these, as shown in fig. 7 (*lig. dent.*), pass medially to the anterior roots. The nerve roots pass through the subarachnoid space and into the intervertebral foramina, each carrying with it a sheath of dura and arachnoid in the normal manner. Those from the eighth and ninth segments are very delicate, and on these rudimentary posterior root ganglia are found, but in the lower segments the roots and ganglia are more nearly normal in size. The position of the ganglia is normal with reference to the intervertebral foramina. The roots from the upper four involved segments (thoracic 7, 8, 9 and 10) pass out directly to their foramina, without descent in the canal, in the manner shown in fig. 8, and diagrammatically in fig. 5, C. The roots from lower segments incline downwards before emerging, and finally those from the lowest segments pass under the closed meningeal sheath of the lower part of the myelocele already seen in fig. 6, at the level of the fourth lumbar vertebra. On dissection (fig. 8), this meningeal sheath is found to be composed of the three fused meningeal layers, which are adherent for a distance of about one millimetre to each other and to the cord. Almost immediately they become separated into their component parts and lose their adherence to the cord, which is closed from this point down. The cord as it passes under the meningeal covering is flattened, but otherwise normal in appearance, and the nerves surrounding it form a typical cauda equina. As will be expected from a study of the diagram in fig. 5, C, the conus is lower in the canal than normal, and the cord terminates at the level of the third sacral vertebra. Except for this the cord and membranes, which at the level of first sacral vertebra become covered by skin, are quite natural after they enter the sacral canal.

Microscopical examination.—Sections were made of cerebellum, pons and medulla, and at various levels of the cord. The fixation of the brain was not sufficiently good to warrant detailed study. The cerebellum has a fairly well-formed corpus dentatum, and the folia, which are few in number, present a definite cortical layer. The pons contains transverse fibres and lemniscus, both myelinated. Cells of the nuclei pontis are not differentiated. In the oblongata the inferior olivary nucleus is well developed, and the medial lemniscus, the emerging fibres of the sixth and seventh nerves, and entering fibres of the vestibular nerve are myelinated and occupy their normal positions. In all the sections there is a looseness of the tissue and a paucity of fibres and cells even where the general structure is most nearly normal; many small areas occur in which the neuroglial meshes are filled with fluid, and in other parts there is an appearance of œdema of the cells. There are many cells which do not appear to be differentiated into supporting and nerve elements; some perhaps represent neuroblasts.

In studying the sections of the cord it will be necessary to refer to the undissected specimen (fig. 6), and to fig. 8 in which the levels of the sections are indicated, and to recall that a "segment" of the cord is numerically determined by the relationships of its nerve roots, and not by its position in the spinal canal. In this case, as had already been seen, the nerve roots behave in a most irregular manner, and it is only by tracing the connections of the section of cord studied that its segmental position can be determined.

Section A (fig. 9, A).—Level of fifth thoracic vertebral segment (first thoracic segment of cord), above lesion. Sections show a normal central canal lined by an ependymal layer. Cells of the anterior horn of grey matter are well formed and their distribution corresponds with that of normal cord of first thoracic segment.

Cells of the posterior horn, difficult to distinguish even in normal cords, cannot be definitely differentiated. It is probable that a small group of them

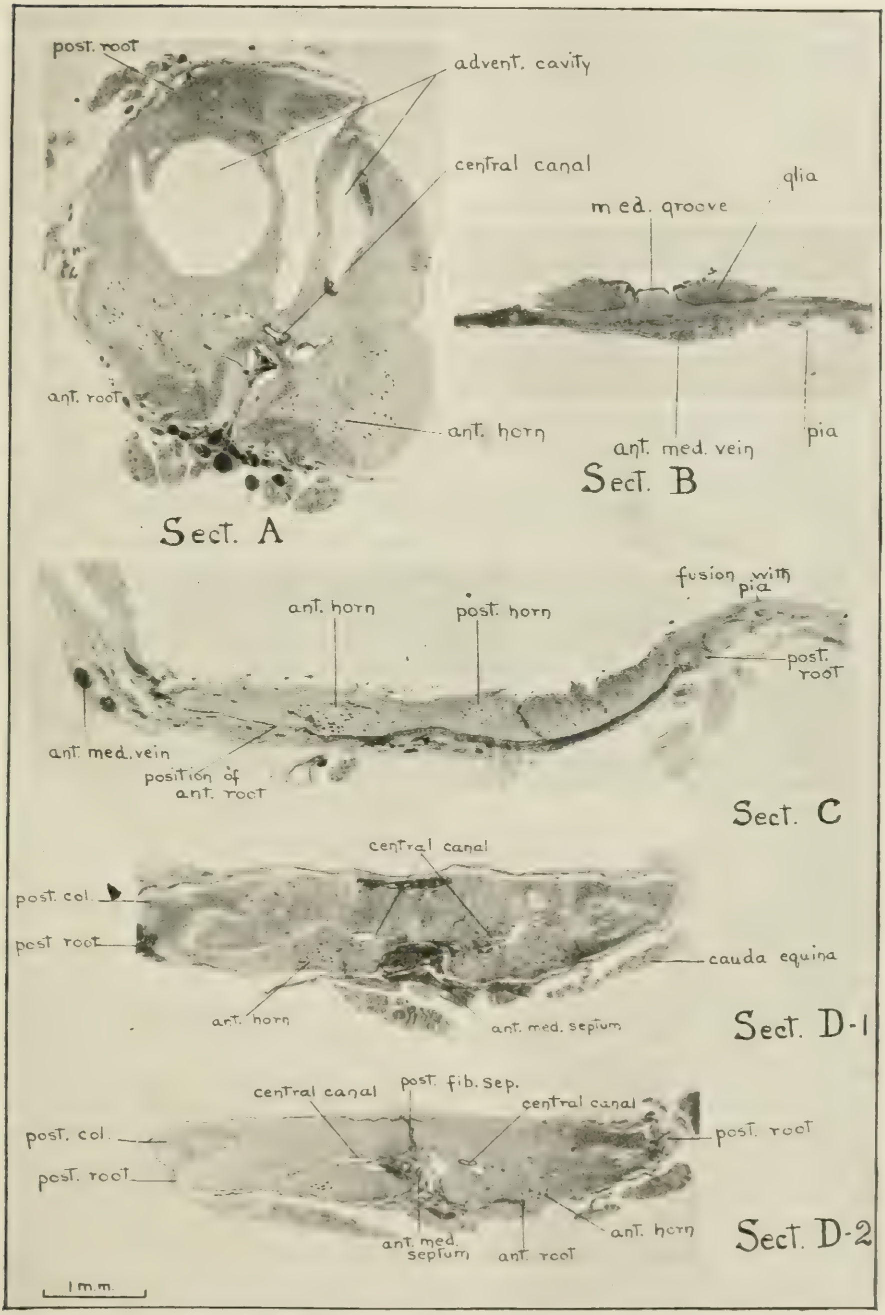

FIG. 9.—Case I, myelocele. Photomicrographs of sections at the levels indicated in fig. 8.

can be made out in the region indicated in the photograph. The posterior portions of the cord on each side are partially replaced by spaces which occupy roughly the position of the posterior columns, the ascending fibres of which have been interrupted in their course by the imperfect development of the cord below. These and similar spaces in other sections to be described are not artefacts, as is evident from the good preservation of the surrounding structures. The ventral cerebro-spinal tract is normal in size and position, and non-myelinated. This tract normally becomes myelinated late in intra-uterine life. No other long tracts can be distinguished. The antero-lateral fasciculi proprii of each side are myelinated; and there are some other scattered myelinated fibres which may be also regarded as association fibres. The surrounding area is composed of neuroglia and of non-myelinated nerve fibres. The anterior and posterior nerve roots are myelinated and occupy their normal position.

Section B (fig. 9, B).—Upper limit of myelocele, level of eighth thoracic vertebra, eighth thoracic segment of cord. At this situation, as shown in the photograph, the cord is represented by a layer of poorly differentiated tissue, two or three cells in thickness (*med. groove*), the open medullary folds. (Compare fig. 1, A). These cells are prolonged for a short distance lateral to the mid-line, but no continuous cell layer can be followed between them and the epithelial surface of the adjoining skin; apparently it has been destroyed in handling the specimen. On either side of this open medullary groove is a small mass of irregular tissue (*glia*) composed of nerve fibres and neuroglia. The tissues beneath are poorly formed pia and arachnoid, and small vessels from these layers penetrate the glial masses; laterally they fuse and pass into the corium. No differentiated nerve cells can be found in any portion of this section. The growth of ascending tracts has apparently been blocked below this region by the adherence of the membrane in the myelocele, but the lateral glial masses undoubtedly contain a few fibres ascending from the cord below. These are in turn blocked at the upper limit of the myelocele with resulting absence of the posterior columns noted in Section A. Similarly the descending tracts are blocked at the upper limit of the defect and only those which are formed in the cord below this level are to be found in lower sections.

Section C (fig. 9, C).—Middle of myelocele, level of twelfth thoracic vertebra (first lumbar segment). At this level the ribbon of medullary tissue shows a remarkable degree of differentiation into its usual fœtal characters. Large anterior horn cells lie near the median line, and a small group of posterior horn cells lateral to them. Small anterior and posterior nerve roots emerge and enter in relation to these cell groups. They are non-myelinated. The substantia gelatinosa is well developed. The remainder of the ribbon is composed of an indiscriminate mass of neuroglia and nerve fibres, none of which are myelinated. The nerve fibres noted in Section B evidently ascend from the cells in this region. The ependymal layer is destroyed, but a depression corresponding with the central canal is found at the median line. The posterior surface is composed of glial tissue and unmyelinated fibres traversed by delicate fibrils of connective tissue coming from the pia and containing capillary vessels. This glial layer extends laterally for a considerable distance, and is probably augmented by fibres from the tracts ascending from below. Anterior to the medullary ribbon the pia lies in contact with the nervous layer; it is thicker than is normal and contains many vessels and some leucocytes. In it lie bundles of nerve fibres, some of which appear never to join the cord but to be lost in the meningeal tissue. Sections from the lower part of the ribbon cord show the same structure, but the nervous tissue is broken up by many minute blood-vessels, and a delicate vascular plexus extends over the whole dorsal surface from one lateral pial margin to the other.

Where the ribbon cord closes and passes under the meningeal layers, serial sections were made in an effort to find the transition stages. The nervous tissue in the upper of these sections is so obscured by penetrating capillaries that little information can be gained from them. In the upper sections the anterior medial septum sends two lateral trabeculæ, which pass laterally; at the end of each there is found a slightly elongated ependyma-lined cavity. It has not been possible to trace the ependymal cells to the surface of the cord in any of the sections. At a slightly lower level the fibrous septa disappear, but the central canal remains double.

Section D-1 (fig. 9—D-1).—The level of this section indicated on fig. 8 is that of the fifth lumbar vertebra, and the position of the nerve roots show that it represents the second sacral segment of the cord. The cord is flattened antero-posteriorly; the central canal is double. Anterior horn cells are well developed; posterior horn cells cannot be distinguished. A small posterior column is present and is myelinated. The anterior and posterior nerve roots are myelinated. The cord contains little else that is recognizable; it is œdematous and broken up by fine vessels. The nerve roots of the cauda equina are disposed round it; those from the ribbon cord above are non-myelinated.

Section D-2.—Level of the third sacral segment, one millimetre below Section D-1. The central canal is still double at this level. Little change has occurred except that between this section and the preceding an adventitious septum of fibrous tissue has extended inward from the posterior pial sheath, and has here met and fused with the anterior median septum, completely bisecting the cord. Otherwise the structure is as before. In sections slightly below this level the fibrous septum once more disappears and the central canal is gradually lost on one side, so that the lower segments (fourth and fifth sacral) of the cord contain but one central canal which is placed slightly laterally.

Various explanations of this have suggested themselves to me. The simplest, and therefore perhaps the most probable, is that the mesoblast-forming pia which is seen in the upper portion of the myelocele slightly elevated in the mid-line under the open medullary groove, has here likewise been abnormally elevated to a sufficient extent to cause bifurcation of the closing medullary tube. The mesoblast does not, however, come into relation with the medullary plates in the normal embryo until these are already closed, but where one structure departs from the normal associated structures follow suit. Moreover, if the closure of the folds were markedly delayed in its relation to other processes, it is feasible that mesoblast would follow the time sequence of other mesoblastic development, and not that of ectoderm, i.e., medullary folds. A double central canal is not a very infrequent anomaly in cords with defects other than spina bifida.

GENERAL DISCUSSION OF CASE I.

Attention is especially directed to four features in this case, viz. :—

(1) The influence of the inequality of growth of cord and vertebræ, and the adherence of cord, producing abnormal direction of nerve roots and abnormal position of cord segments in the canal.

(2) The formation of spinal ganglia and nerve roots in segments in which closure of the tube has not occurred.

(3) The absence of histological differentiation in certain of the involved segments, and the normal histogenesis in other segments which are morphologically defective.

(4) The imperfect development of segments above the lesion due to mechanical hindrance.

CASE II.

Myelo-encephalocele—rachischisis completa totalis of Class 3 (B).

Specimen No. 1133, University of Texas Pathological Museum.

No complete account of the state of this specimen will be given in the present communication, but certain points in the spinal part of the defect are of value in the interpretation of the other cases under consideration. To these the description will be limited.

Description.—This specimen belongs to the general class of anencephalic monsters, of the type in which there is posterior cleft of the calvaria and spinal column. The mouth and nose are normal, the eyes bulge in the manner characteristic of this type of monstrosity; the forehead is low. The ears are normal in shape, but are situated close to the shoulders, and the chin is drawn down upon the sternum. This position is frequent in anencephalic monsters and indicates the absence or imperfect development of the cervical region, which is a usual accompaniment of the cranial and spinal defect. The general appearance of the body is otherwise normal, and the age about seven (intra-uterine) months.

The specimen shows posterior cranioschisis with protrusion of an imperfectly formed brain enclosed in a pia-arachnoid sheath; the dura covers the base of the skull and extends over the edge of the defect to blend with the skin of the anterior part of the head. The mass of brain tissue extends caudalwards and overlaps the upper part of the bifid spinal canal. Examination of the upper part of the spinal column shows that all the cervical vertebræ are lacking, and the upper two thoracic vertebræ are either lacking or abortive, as are the cord segments corresponding to these. No attempt has been made at the present time to study the other defects of the cervical body segments. All the ten thoracic vertebræ which are present are cleft; the spinous processes and the laminæ are normal in size, but flare outwards as do those in the affected area in Case I. Examination of the thoracic region shows that ten ribs are present, articulating normally with the thoracic vertebræ; and a cursory examination of the contents of the body cavities reveals nothing abnormal. The upper four lumbar vertebræ are flaring; the fifth has an incomplete arch, which is bridged by a fibrous band. The sacral vertebræ are defective in the spines only. The open vertebral groove is covered by meningeal layers from the base of the skull to the level of the fourth lumbar vertebra. At this level the meninges form a closed tube and pass into a zone of imperfect parchment skin, which blends at the level of the fibrous arch of the fifth lumbar vertebra with skin which is in all respects normal.

A ribbon cord similar to that described in Case I extends from the brain above to the level of the first lumbar vertebra below. Here it passes into a normal filum terminale which is prolonged under the meningeal layers into the sacral canal. The cord in a fœtus of this age (seven months) should end at the level of the third lumbar vertebra. The slightly higher level assumed by this cord is apparently due to defective growth of its segments; it is greatly exaggerated in appearance in the undissected specimen because of the disproportion of the spinal column owing to absence of cervical segments. It is important to note that the entire cord is cleft; the coccygeal nerve arises, as do the nerves proximal to it, from a ribbon of medullary tissue. The lower nerve roots are grouped about the ribbon cord from which they arise, and pass under the meninges at the level of the fourth lumbar vertebra. Here the meningeal layers form a closed tube which passes under parchment skin as described above.

Discussion.—The features of this case which have a bearing on anatomical characteristics of spina bifida restricta are the only ones to which attention is now called.

(1) The "upward migration" of a cord all the segments of which have failed to close.

This appears to be due to the absence of any abnormal adhesions between neural tube and surface ectoderm in this particular case. The formation of the filum terminale indicates that the adherence of the last coccygeal segment (rudimentary) has been normal.

(2) The formation of the lower vertebral segments, which has been carried on to a considerable extent after the upward migration of the corresponding open cord segments. The vertebral laminæ should be fused in the eleventh week, while the migration of the cord does not commence until after the twelfth week. In the lumbar and sacral

regions, however, the completion of the vertebral arches is later than in the thoracic. In this case development progressed as soon as the ribbon cord slipped out of the way. This shows to some extent in Case I, but less strikingly because the complete cord defect in Case I does not extend below the second sacral segment, the segments below this being closed. In Case II, the entire neural tube is open, including the first coccygeal segment, i.e., the last segment which attains adult development in man. The fifth lumbar vertebra has, however, developed a fairly normal arch and the sacral vertebræ are deficient in spinous processes only.

The meninges attached to the lower segments of the open cord have been carried upward by the ascending cord, and the surface ectoderm has developed into normal skin over those vertebræ which possess reasonably normal arches, i.e., as high as the fifth lumbar.

These points will be found to throw light on certain obscure features of cases with defects restricted to the lumbo-sacral region.

CASE III.

Cystic myelocele—rachischisis completa restricta of Class 3 (A).

History.—M. E., female, aged three months, John Sealy Hospital.

Family history negative as regards physical defects. This, the first child of this family, has been weakly since birth, and has had constant digestive disturbances. She appears to be normally developed except for a lumbar "meningocele." Five days before admission to Sealy Hospital she had a febrile attack, which terminated three days later, when the upper part of the meningocele ruptured. Pre-operative condition: Examination showed that there was a meningocele occupying the lower lumbar and upper sacral region, covered by typical parchment skin partially collapsed and ulcerated, of a diameter of about one and a half inches. A minute opening was present at its upper part, not in the mid-line, and from this cerebrospinal fluid flowed freely. There was no visible sign of nervous elements on the parchment surface, and the opening did not appear to be a central canal. There was, however, evidence that the condition was not confined to the membranes, as the legs were partially paralysed and there was incontinence of urine and fæces. In a position of rest the legs were kept extended at hip and knee, and no movements of the feet were observed. The thighs were flexed feebly when the baby was disturbed. At the time of admission there was diarrhœa, but careful dressing and attention to cleanliness caused great improvement in the condition of the rectum and in the ulcerated surface of the meningocele. Any handling of the child, and especially touching the sac, produced evacuation of the bowels and bladder. Complete collapse of the sac occurred from time to time, and at these times the child was restless and distressed. The flow of cerebrospinal fluid remained constant. Operation by Dr. J. E. Thompson, July 8, 1919, under ether anæsthesia. From the start the baby took the anæsthetic badly and artificial respiration had to be resorted to before the commencement of the operation. After this preliminary trouble, however, the respiration, though weak, was regular, and the heart fairly strong. A transverse incision was made and the sac opened. The filum terminale and a pair of nerve filaments were found to be spread over the lower extremity of its inner wall and these were removed with this portion of sac wall. Attached to the middle of the sac was the termination of the cord with its nerve trunks running down across the cyst into the foramina. This terminal portion of cord was cut across and the central canal found to be rather large, horseshoe-shaped and attached to but closed by the parchment skin of the sac. This was about the level of the first sacral vertebra. Above and below this point the parchment skin merged with a wall of well-formed dura, which was dissected free on each side and the edges sutured over the cord with chromic gut stitches. The remaining parchment was dissected till normal skin was reached and this was sutured. The baby left the table in a serious condition of shock and within the next hour developed feeble convulsive movements of the whole body, including the legs

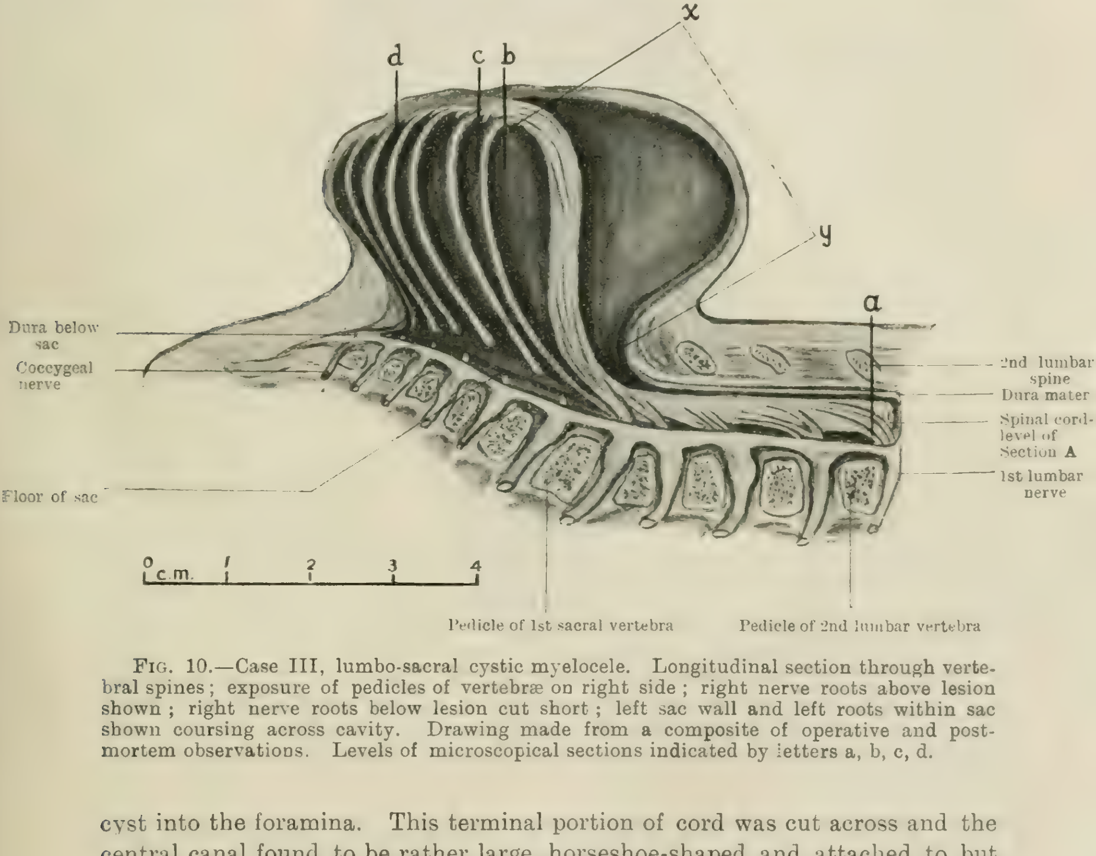

FIG. 10.—Case III, lumbo-sacral cystic myelocele. Longitudinal section through vertebral spines; exposure of pedicles of vertebræ on right side; right nerve roots above lesion shown; right nerve roots below lesion cut short; left sac wall and left roots within sac shown coursing across cavity. Drawing made from a composite of operative and post-mortem observations. Levels of microscopical sections indicated by letters a, b, c, d.

and feet. Death occurred within three and a half hours after the completion of the operation. Only a partial autopsy could be obtained and had to be limited to the affected area, so that observations on the condition of the internal organs and upper part of the central nervous system are unfortunately lacking. The lower four lumbar vertebræ, sacrum and coccyx, were removed in their entirety with the surrounding tissues.

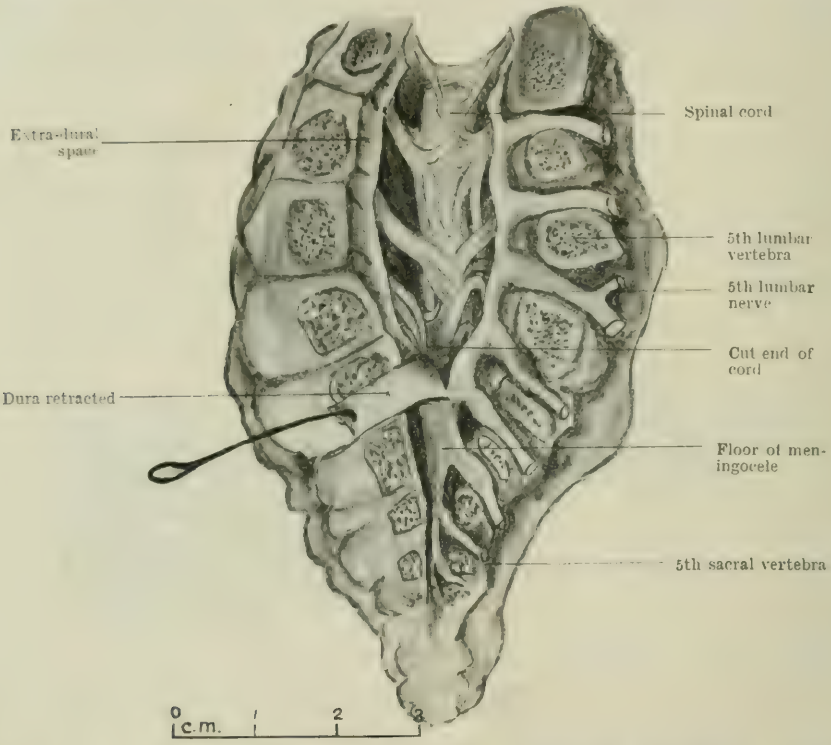

FIG. 11.--Case III, lumbo-sacral cystic myelocele. Dissection of specimen as removed post mortem. Bodies of vertebræ split in anterior median line, exposing cord from its anterior aspect. On the left side the vertebræ have been further dissected to show the pedicles.

Description of myelocele.—For the sake of clearness the description here given, like the accompanying diagram of the longitudinal section (fig. 10), will be a composite of operative and post-mortem observations. The sources of the information on each detail will be readily seen, but any attempt to separate the two sets of findings complicates the discussion unnecessarily. The laminæ and spine of the second lumbar vertebra are normally developed. The pedicles and transverse processes of the vertebral arches of the third and fourth lumbar are normal, but the laminæ and spinous processes flare outward, the vertebral foramen being closed dorsally by a dense fibrous band extending between the bases of the arches. The fifth lumbar has no such band, but presents a widely open foramen. The laminæ and spines of all the sacral vertebræ are flaring and no fibrous band is developed.

Overlapping the third and fourth lumbar vertebræ, but not connected with them, is a thick meningeal sac which extends downward as far as the lower end of sacrum. This sac is covered by " parchment " of unusual thickness, which at the periphery is found to be composed of thin integument blending with a very dense dura, two or three times as thick as normal, which is in contact with a thin arachnoid. The subarachnoid space is filled with fluid. At the lower border of the fibrous neural arch of the fourth lumbar vertebra the meningeal layers of the sac are continuous with the sheath of the cord above, and the integument passes into the normal skin of the back. From beneath this fourth arch the cord emerges and passes dorsalward through the sac, surrounded by small nerve roots which are held in close contact with it by the pia. At a point a little below the middle of the sac the end of the cord becomes attached to the inner surface of its dorsal wall, and lower down is inseparably blended with it. Near the mid-line of the sac the dura fuses with the skin, and cannot be lifted from it though it retains its characteristic shining inner surface. The pia cannot be followed by the naked eye below the point of attachment of the cord, but at its lower end it is considerably thickened, and just below this it fuses with the other meningeal layers. From this point down to the lower limit of the posterior wall (roof) of sac, these fused meningeal layers form a definite band of dense white fibrous tissue which projects into its cavity. This band is augmented by the nerve-roots which are carried down along the cord, and also, as will appear later, by some poorly developed cord tissue. It is possible that in the tense condition of the unruptured sac this thickened band would have been apparent from the external aspect, and might have served as a clue to cord attachment. Below and laterally to the point of attachment of the cord numerous nerve-roots are seen passing from the inner surface of the roof of the sac traversing the cavity toward the intervertebral foramina. The upper and larger of these nerve-roots pass freely across the cavity, but the lower smaller roots run caudalward along the roof and then pass upwards a short distance on the floor of the sac in the substance of the arachnoid layer, which here is closely approximated to the dura. More careful study reveals the fact that those nerve-roots which arise from the saccular portion of the cord above its attachment to the sac wall, pass upward along the cord and enter foramina at a higher level than their point of origin.

In order to verify these observations, the anterior wall (floor) of the sac and that part of the cord above the lesion which had been removed after death, were exposed from in front by removing the bodies of the vertebræ. As is shown in the drawing of this dissection (fig. 11), not only the roots that arise from the intracystic part of the sac, but those which arise from the cord above the lesion, are found to course upward in the spinal canal before passing into their foramina. By a careful study of the relationships of the undivided nerves above the operative section (B, in fig. 10) and of the divided nerves in the lower part of the sac, it is possible to determine that all the sacral roots and the coccygeal nerve were attached to the sac wall and were divided with it, and that the lower radicles of the fifth lumbar, as shown in fig. 10, were similarly adherent to the sac wall, but the upper radicles of this pair of nerves arose from the cord at some distance from its attachment to the sac, and passed up it to the foramina without interference from sac wall. Passing upward and examining the part of cord in the normal canal above the sac, one finds that the upward inclination of the roots decreases, but is still evident at the upper limit of the specimen, the roots from the level of the third lumbar vertebra passing through the twelfth thoracic foramen.

In fig. 11 it will be noticed that the nerve-roots exposed to view are somewhat curved owing to the relief of tension when the cord from which they arise was cut free from the sac wall at operation. This also accounts in part for the apparently small number and great thickness of the individual radicles as compared with the numerous delicate fibres found in normal cords. So soon as they have reached the floor of the sac the relationships of dura and of spinal ganglia and nerve trunks are entirely normal, and the anterior and posterior primary divisions of the sacral nerves pass through well formed foramina in the usual manner, though the position of the posterior foramina is obscured by the flaring vertebral laminæ. It is evident, therefore, that the cord must have lain in contiguity with the vertebral rudiments when these structures, the roots and ganglia, were developing, as the normal connections could not have been established across a large cavity filled with fluid. The fluid collection in the subarachnoid space must, therefore, have occurred after these connections were made, and may be a result of the impairment of arachnoid function caused by the adhesions at the mid-line already mentioned.

The upward direction of the nerve roots to their foramina of exit is due to two factors. To one of these reference has already been made in discussing Case I, and attention is again called to fig. 5, in which the normal cord migration and its modification in Case I is represented. In the specimen now under consideration the first sacral segment of the cord was held in contact with the skin so that it could not slip upward in the spinal canal as this elongated. Consequently the cord between this point and the fixed first cervical segment was stretched to the full length of the enlarging canal. Were this the only force at work the stretching would have been uniform throughout the length of the cord and the nerve roots would have continued to pass out horizontally to their respective body segments. However, the distension of the meningeal sac with fluid still further stretched the lower segments, so that they became actually longer than the spinal canal by the distance "x-y" indicated in fig. 10, and the nerve-roots above the point of cord attachment were carried below their foramina of exit to this extent, and so appear to ascend in the canal before emerging. This is shown diagrammatically in fig. 5, D.

The position of the roots below the adhesion of cord to sac is determined by the same two factors, the fixation of the second sacral segment and tension by the sac, acting under different conditions. It must be remembered that in the normal migration of the cord, elongation of the roots takes place *pari passu* with the elongation of the canal, and the cord itself is never submitted to strain. In the meningocele, however, the tissues of the cord itself are stretched, and it seems possible that this may increase the minute histological defects found in these cases and so increase the amount of functional loss.

Microscopical examination.—Sections were made at the levels indicated in fig. 10. The region from the point of attachment of the cord to the end of the visible nervous tissue (*b* to *c* in the diagram), a distance of about four millimetres, was examined in serial sections, and those which are of the greatest interest are described. The transitional stages as illustrated in the intervening sections in the series are referred to between the descriptions of the separate sections photographed.

Section A.—Cord above the lesion (fig. 12, A) : This was removed from the level of the second lumbar vertebra, but the relations of its nerve roots show that it represents the twelfth thoracic segment. The arrangement of the motor cells is not that of the lumbar enlargement. The shape of the cord in section is roughly pyriform, with the wide part anterior, and a depression on each side posterior to the anterior horn. The anterior median fissure is shallow, the anterior commissure normal. The central canal is narrow just above the septum, and posterior to this has two wing-like projections irregularly lined by ependyma. It then passes posteriorly and can be followed by means of its ependymal lining to within a short distance of the posterior surface. In the section photographed no posterior median septum is present, but in sections from the same block of tissue slightly proximal to this the central canal blends with a definite posterior glial septum. Anterior horn cells are few in number, but well developed ; posterior horn cells cannot be identified with certainty, but a few nerve cells corresponding in shape and size with them are present in the region indicated in the photograph. The neuroglia in the whole section is loose in arrangement and œdematous, and contains an excess of small blood-vessels. Posterior nerve roots enter near the posterior mid-line ; their ascending fibres form a small posterior column which is normally placed. Other myelinated fibres from these roots pass round the distorted central canal to end in relation to the cells of the posterior and the anterior horns. On the left side other myelinated fibres which have ascended for a short distance in the posterior column are seen passing round in the same manner to the cells of the grey horns.

Anteriorly there is a quite normal distribution of myelinated fibres representing tracts which cannot be definitely differentiated from one another in a normal cord of this age. The antero-lateral fasciculi are very prominent. An area of less definite myelination probably represents the lateral cerebrospinal bundle. On the left side of the section there is a group of cells (*sub-gel.*), which probably correspond to the gelatinous substance. On the right side there is no similar group in this region but there is a less definite group in relation to the entering fibres of the posterior root. It will be recalled that the gelatinous substance normally lies as a cap on the posterior horn, between it and the entering fibres. One or two myelinated fibres cross in the anterior commissure. There is an appearance of crossing fibres in the posterior commissure, but a careful reconstruction from the study of many sections from this area shows that these are fibres from the homolateral posterior column passing round the dilated central canal. The collapse of the central canal has caused a tear in the posterior part of the cord to the left of the median line, and the relations of structures in this region are much altered by the distortion. This has rendered the interpretation of the findings exceedingly difficult, but could not be avoided as it was the result of the operative procedure. In the uncollapsed specimen the central cavity must have been nearly circular, with its posterior wall composed of glia and nerve fibres and its anterior wall of the grey horns and anterior part of the white matter.

Section B (fig. 12, B).—This section is taken at the lower end of the cord, just before its attachment to the sac wall. The distribution of the nerve radicles from this shows that it represents the first sacral segment. Owing to the obliquity of the attachment to the sac wall the section shows a great enlargement of the cord in an antero-posterior direction. The transverse diameter is about normal. There is a well-marked anterior median fissure but no definite posterior median septum. The central canal is enormously enlarged and irregular in shape; its walls are collapsed as a result of the operation. The ependymal layer is present in the anterior portion of the cavity, but is lost posteriorly. This is the case in all the sections of this region, and appears not to be an artefact but to indicate a communication of central canal with an adventitious cavity.

In the substance of the medullary tissue are a few small collections of fluid, and the nervous elements present a loose arrrangement, presenting evidence of œdema. There is in many places an apparent absence of nerve cells or fibres lying between the meshes of glial fibrils, and there are but few neuroglia or neuroblastic cells. Round the central canal there is a tendency for the cells to be spindle-shaped and to retain somewhat the type of the spongioblast of the mantle layer of the embryonic cord. In the posterior region there is no trace of posterior horn cells, but posterior nerve-roots are myelinated and enter normally. In the anterior horn there is a well formed group of cornual cells of normal size, corresponding roughly in arrangement to those of lumbar enlargement, and the emerging motor fibres are myelinated and numerous, but somewhat irregularly grouped. The antero-lateral fasciculi proprii are myelinated and normally placed; no other tracts are distinguishable. The membrane covering this part of the cord is thicker than normal; and though laterally and anteriorly it appears to be composed of inflammatory pia only, posteriorly it blends with a dense layer which represents fused arachnoid and dura. Posteriorly also there is much leucocytic infiltration, probably due to the proximity of the inflamed sac wall.

Immediately below this section the cord was so fimly adherent to the sac

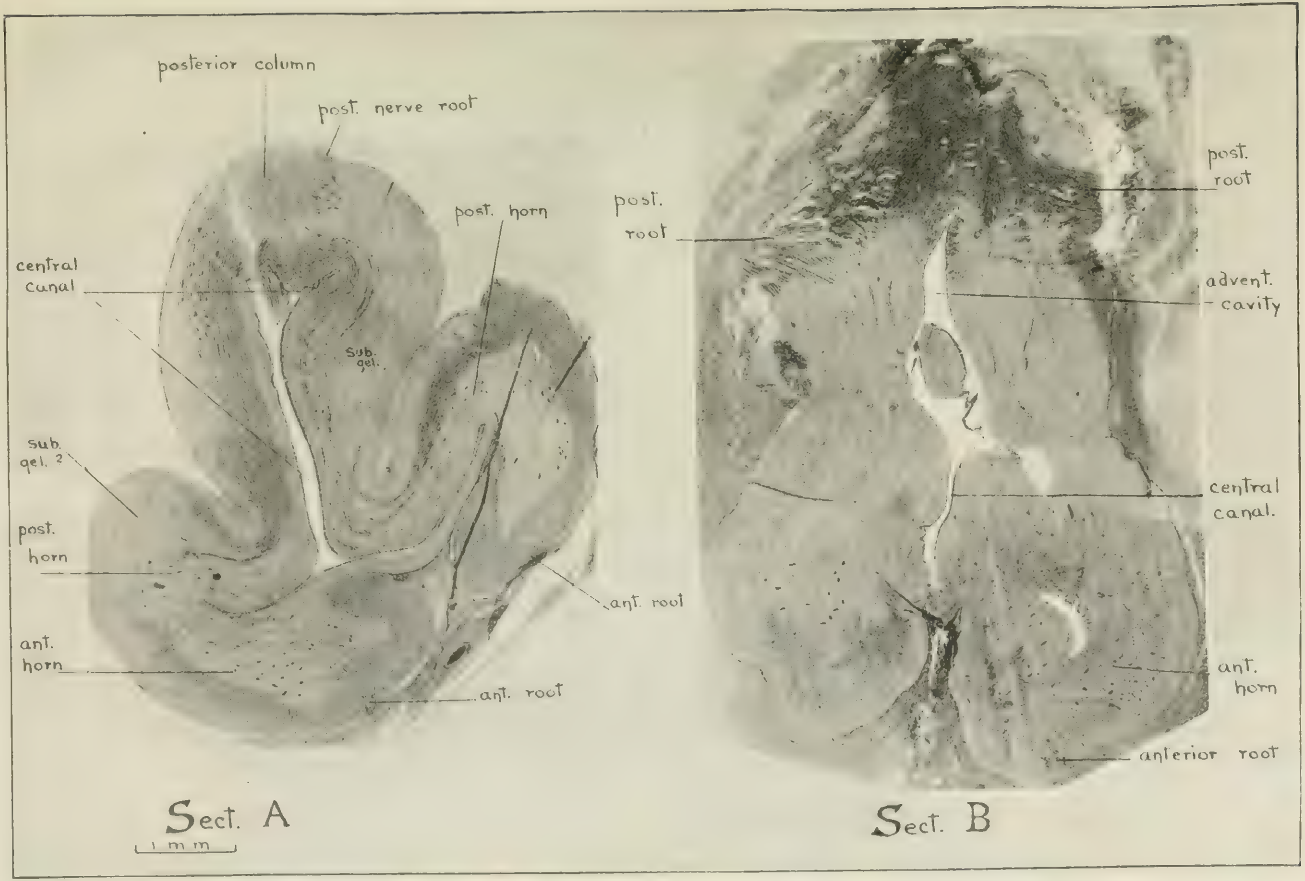

FIG. 12.—Case III, lumbo-sacral cystic myelocele. Photomicrographs of Sections A and B at the levels indicated in fig. 10.

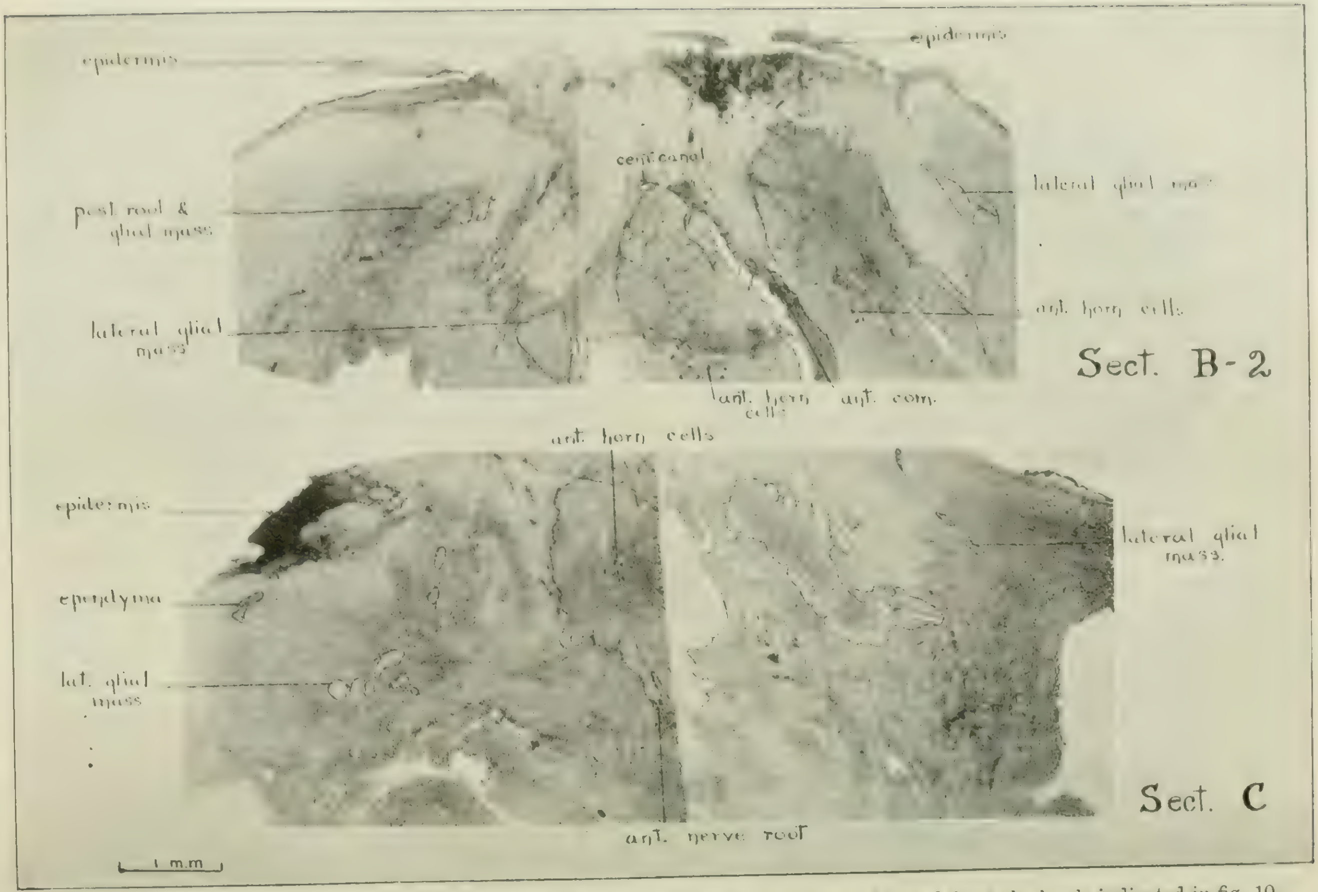

FIG. 13.--Case III, lumbo-sacral cystic myelocele. Photomicrographs of Sections B.2 and C, at the levels indicated in fig. 10.

wall that sections were made through this in order to preserve the posterior portion of the cord tissue. The first of the serial sections examined from this region (between B and C on fig. 10) shows that the posterior part of the cord is spread laterally as it becomes attached to the wall of the sac, and the adventitious cavity in Section B enlarges and approaches the surface. In the posterior attached portion less and less nervous differentiation remains, so that in the distal sections it appears only as a glial mass lying in the subcuticular connective tissue layer. This glial mass is separated into two parts by the extension of a fibrous band through the posterior median line towards the anterior median septum. In more distal sections this band of adhesions spreads into the posterior cord tissue laterally, and finally breaks it up into small, partly differentiated, neuro-epithelial masses. At the same time, the central canal persists in the anterior part of the cord but narrows as it approaches the posterior surface. The anterior median septum extends dorsally until it finally reaches and becomes fused with the subcuticular layer of fibrous tissue, thus separating the anterior portion of the cord into two lateral halves. In each of these a prolongation of the central canal persists for a time. In one of them it is carried somewhat more caudally than in the other. On account of the obliquity of the cord in this situation the interpretation of the sections is by no means easy.

Section B-2 (fig. 13).—The position of this section is half-way between B and E as indicated on fig. 10. There remains but little of the posterior part of the cord, and only in scattered masses close to the surface epithelium. At the median line the surface epithelium is thinned and in some sections absent, and beneath it there are many inflammatory cells in the fibrous tissue which separates it from the cord substance. The anterior part of the cord, recognized by a few motor cells, is separated into two halves by the adherence of the anterior median septum to the surface fibrous layer. The depth of this fibrous bridge and of the nervous tissue is increased by the obliquity of the section. At the point indicated in the photograph there remains a trace of the anterior commissure which persists for a few sections below this point and then disappears. No myelinated fibres are present except a few in the anterior part of the cord coming from anterior horn cells. The anterior roots and the extreme anterior part of the cord have been cut off by the removal of Section B. The posterior roots are non-myelinated and consist of but few nerve fibres with an excess of fibrous tissue; they lie close to the surface epithelium and are lost in the fibrous subcuticular layer before they reach the cord. At the left in the photograph (*cent. canal*) there remains a small ependymal-lined cavity, the prolongation of the central cavity of higher sections. This is carried farther down on the left than on the right side. Both the nervous masses are connected with the thinned epidermis by strands of undifferentiated epithelium, infiltrated with inflammatory cells. The nervous masses are considerably broken up by adventitious connective tissue trabeculæ and by inflammatory material. The condition here recalls Case I, fig. 9, where the ribbon cord passes into the closed distal segments. In

Case I, the transition is not obscured by adhesion to skin, and the bifid character of the central canal is more easily seen. In these the open segments are adherent to skin, and the relations are so altered that the stages are difficult to recognize.

Section C (fig. 13, C).—In this section the anterior part of the cord is still recognizable; one or two anterior horn cells are present in each lateral mass. On the left side an anterior nerve root emerges, but it contains no myelinated fibres, nor are there any in the anterior cord rudiments. Posteriorly irregular epithelial strands connect the nervous masses with the surface epithelium. (The loss of epithelium over the middle portion of the photograph is an artefact.) Laterally there are many small collections of partly differentiated neural epithelium, which appear to represent the posterior portion of the cord. On the left side one of these contains a cavity with a well developed ependymal lining, which has no connection with any other; it persists for but a few sections proximal and distal to this level.

In the remainder of the serial sections from this region the posterior (lateral) collections of neuro-epithelium become more and more attenuated and invaded by the surrounding fibrous tissue; the anterior masses remain recognizable for some distance, and are still present in the next section to be described.

Section D (not photographed).—At a distance of 10 mm. from Section C. The anterior masses are distinguished only by their position and relation to those in higher sections. No motor cells are present, yet nerve-roots approach close to the deep surface of the nervous tissue, and at certain points there appear to be emerging bundles of non-myelinated fibres. Between the integument and the neural masses there still persists an irregular and broken epithelial connection.

For a short distance below the last section nervous tissue is demonstrable, and nerve bundles are present in the connective tissue to the caudal limit of the sac wall.

CASE IV.

Cystic myelocele—rachischisis completa restricta of Class 3 (A).

History.—M. E. H., female, aged three weeks.

Father and mother healthy, except that mother has a "weak back," but had no trouble while carrying child. Baby has one brother, aged 6, who had "infantile paralysis" at age of 1½ years, which has left his legs weak, though all the muscles seem to be equally developed. His sphincter control is normal. No examination of his back was made. No history of congenital defect in other members of either side of the family.

Description of condition.—Baby well formed, except for spina bifida. Nutrition good; no hydrocephalus apparent. In lower lumbar region is a tumour size of half a mandarin orange, covered by parchment skin, ulcerated on the surface and covered by a transparent dressing. On removing this the ulcerated area bleeds, but shows no purulent discharge, nor spinal fluid.

Pressure near or on sac causes the baby to cry. Urination and defæcation occur frequently, especially when the child cries or the sac is touched. Movements of thigh are normal. In a position of rest the legs are kept straight, but passive plantar flexion causes slight active flexion of the knees. The feet lie in a position of flaccid semi-extension, and the usual "curl" of a baby's foot is absent. If the foot is irritated the extensors act so as to pull it into a position of dorsiflexion on the ankle, but the toes seem not to move. No response of any kind could be obtained to tickling sole of foot or pressing calf muscles. No attempt was made to determine the state of sensation in the thigh or perineum. Pre-operative diagnosis: meningocele: position of cord not determined unless indicated by ulceration of surface. Muscular responses probably indicate that the tibialis anterior (L. 4 and 5 and S. 1) and extensor longus digitorum (L. 4 and 5 and S. 1) are approximately normal. Peronei (L. 5 and S. 1) and small muscles of the foot (L. 5 and S. 1 and 2 and 3) are involved to some extent. Gastrocnemius and soleus (L. 5, S. 1 and 2); and the urethral and anal sphincters (S. 1 and 2, 3 and 4, Dejerine) are apparently completely paralysed. It seems probable that all the sacral nerves are affected; that the fifth lumbar is slightly so, and that the fourth lumbar is normal.

Operation by Dr. J. E. Thompson, October 30, 1920, under ether anæsthesia. Baby had irregular respiration from the time sac was opened until close of operation, but colour remained fair. Transverse incision. Parchment skin removed, cord found to be rather large at its termination, and to be attached to the sac at the middle where ulceration had taken place. The cord was cut free as close to sac as possible, and its end ligated. It was ovoid in shape and presented a rather large cavity. The level of its attachment was about opposite the fourth lumbar vertebra. Across the sac several large nerves coursed, and two of these on each side passed along cord to the roof of sac to which they were attached by delicate fibrous bands. These were separated, but it was thought that in cutting the cord at its attachment the roots of these were severed. One or two very fine nerve filaments were cut from the lower part of the sac roof below attachment of cord, which probably belonged to the lower sacral or coccygeal. It was impossible to separate these, and their roots had been necessarily cut with the end of cord. Dura and skin were separated at the side of sac and the wound closed in two layers, with a small gutter drain at one end under skin. Post-operative course, October 30, 1920: Condition remained good during day of operation, though the baby had one or two attacks in which the face became cyanotic, but the rest of body remained of good colour. Respiration appeared good during the attacks, which lasted fifteen or twenty seconds. These attacks continued to come more frequently and to be more severe, with irregular respiration. On November 1 the tube was removed from the wound, and was followed by considerable leakage of spinal fluid. This continued to drain profusely for some days, then became gradually less, but was still slight when baby was discharged. During the remainder of this day (November 1) baby took no nourishment; had twitchings of the face and jerking of the eyes to the left (it was lying on the right side). These attacks of facial twitching became increasingly severe. They were at first accompanied by cyanosis, but this became less though the nervous phenomena increased. Attacks occurred whenever the child was disturbed or there was much noise. After an attack the baby seemed worn out, and would drop into a troubled sleep. On November 3 she seemed to regain strength, cried normally, and took some nourishment; but still had some attacks of facial twitching and slight cyanosis. Spinal fluid was draining freely from wound. November 4: had a severe attack of dyspnœa with twitching of the face, mouth, and eyes, and mild general convulsions. Attacks of this nature occurred frequently from 7 p.m. to 10 p.m., and then became less frequent and severe. November 5 and 6: had similar attacks, but of decreasing frequency and severity. On November 7 she had no severe attacks and was nursing better. Drainage from wound was slightly turbid and yellow for the first time. Similar discharge occurred for the next three days, after which there was only a slight drainage of clear cerebrospinal fluid. On November 11 "nervous attacks" ceased entirely, and from then on the baby's condition steadily improved. She left the hospital a few days later. Immediate operative result: No change could be seen in the muscular power so far as it could be determined after the operation. The nurse and the mother said that the big toe and the second toe were extended from time to time, but this was never observed by Dr. Thompson or the writer.

Description of the myelomeningocele.—In this case it is only possible to give the operative findings and the description of the sac as removed, so that all information regarding the cord above the lesion and accurate data regarding the relations of nerve roots and floor of sac are lacking. As viewed at operation, this case vividly recalled the appearance of Case III, and if the reader will refer to the diagram (fig. 10) of that case, the description of the conditions found in this case will be much more intelligible. The conditions found at the operation were: the end of the cord was rather large and distended with fluid, and attached to the sac at its mid-point, which in the distended condition of sac was thought to lie about opposite the fourth lumbar vertebra. Across the sac several large nerve roots passed, and two of these on each side ran along the cord, apparently attached with it to the roof of the sac. Below the attachment of cord one or two fine filaments were seen passing down from the roof of the sac to its floor; they were thought to represent the lowest sacral and possibly the coccygeal nerves.

Roof of sac: Immediately after the operation the removed area of sac was pinned out on cardboard, so as to preserve as nearly as possible its size and shape. It is very nearly circular, measuring $6\frac{1}{2}$ cm. by $6\frac{1}{2}$ cm. in the long and transverse diameters, and when seen from the posterior aspect (i.e., the external surface) all of this except a central area of about 5 mm. was found to be parchment skin, the peripheral area being covered by thin, fairly normal integument. The anterior aspect (fig. 14) is found to be clothed with a shining dura, which is inseparable from the surface layer, and within this is a delicate arachnoid layer. Two and one-half centimetres below the upper limit of sac the cut end of the spinal cord is found, and from this point downwards, as is shown in the diagram, there extends a band of tissue 16 mm. in thickness at its broadest part, and narrowing slightly as it reaches the end of the sac. This band is irregular in shape, and somewhat hemorrhagic where it is continuous with the end of the cord, but below this region it is flat, shining, and rather sharply marked off from the remainder of the sac by two longitudinal bands of fibrous tissue. A vein which runs down the middle line of the band conforms in appearance with the anterior median vein of the cord. On the edge of the band the arachnoid appears to blend with the pial layer which covers it. Apparently the two lateral fibrous bands represent the ligamenta denticulata, but none of the lateral denticulations could be seen. In the upper portion of the median band, medial to the ligamenta denticulata, it is possible to find a few delicate nerve filaments representing anterior roots proceeding outward and upward on the sac roof, and apparently cut off with the end of the cord. These cannot be found in the caudal 25 mm. of the band. Lateral to the ligaments, nerve filaments (posterior roots) can be found lower down, to within 10 mm. of the end of sac. These filaments are very delicate and lie free in the sac; they do not arise from the cord above, but directly from the band of tissue just described. If the inference drawn at operation be correct, that these two roots are the fifth sacral and coccygeal nerves, by counting back from these it should be possible to determine with more or less accuracy the segment of cord attached to the sac. This is probably the first sacral or fifth lumbar, and the clinical examination appears to corroborate this. The presence

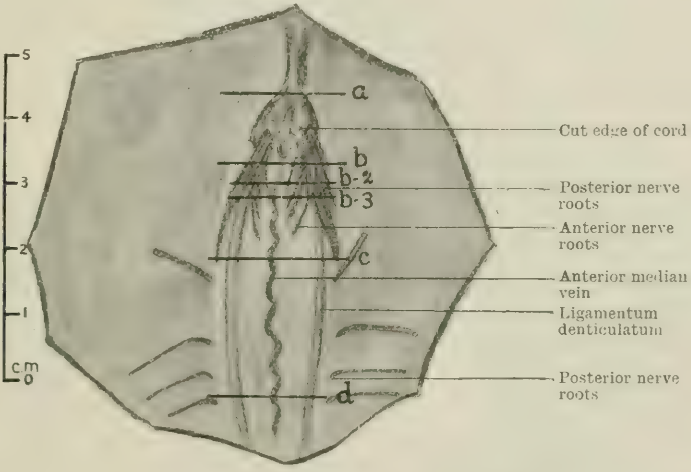

FIG. 14.—Case IV, lumbo-sacral cystic myelocele. Interior of sac as removed at operation, showing band of altered cord tissue, and the region of cord attachment. Levels of microscopical sections indicated by letters a, b, c, d.

of these nerve roots would lead one to expect to find nervous tissue in the median band as low down as the last pair of roots, but by the naked eye nothing resembling normal cord tissue can be seen below the point where the cord has been cut obliquely free from the sac wall. A section immediately below this point, through the sac roof, shows a soft cystic friable mass of tissue, and sections below this reveal only a pink, soft mass of tissue, slightly thicker than the rest of the sac wall, extending laterally a little farther than the band of tissue described on the inner surface, but having no resemblance to cord tissue. As will be seen, however, the microscopic examination of sections through this region are not disappointing.

Microscopical examination..—The sections described were made at the levels indicated in fig. 14, through the median band. The end of the cord had been severed by the operative procedure so close to the sac wall that no section of it could be made before its attachment to sac. At its point of attachment serial sections of the entire region were made, and the photographs are selected from these. The area so examined extended from A to C in the diagram ; the changes observed in intervening sections of the series are noted between the descriptions of the individual sections.

Section A (fig. 15).—This was taken proximal to the point of cord attachment, but the lower sections of the block show a small part of the cut surface of the cord. The surface is covered by thin, stratified, cornified epithelium, below which is a dense layer of connective tissue, representing fused corium and dura. Below this laterally is a thin layer of connective tissue covered by endothelium, the arachnoid, which, thickening as it nears the mid-line, becomes blended with the pia and lies in direct relation to the posterior part of cord tissue. The upper limit of the adherent portion of cord is here seen represented by a mass of glia, in which no nerve cells nor myelinated fibres are present. The anterior part had been cut away in the operation.

Section B (fig. 15, B).—This section is taken immediately distal to the point of cord attachment, and is the first of the series through the region which has not been affected by the operative incision. It is probable that it represents the first sacral segment of the cord (cf. gross description). As will be seen in the photograph, the surface here is covered by a thin layer of stratified squamous epithelium, imperfectly cornified, and having none of the normal skin glands nor papillæ. Immediately below it is a mass of connective tissue which is in parts densely infiltrated with leucocytes and with blood.

Below this layer of connective tissue there is a dilated cystic cord, of which the anterior portion only bears any resemblance to normal cord structure. Laterally the subcutaneous connective tissue is found to blend with an imperfect dural and arachnoid layer, but in the region where nervous tissue exists these are not present. The cord anteriorly is clothed by a thick layer of vascular connective tissue, apparently a thickened outer layer of pia mater in which lie nerve roots ; and within this is a delicate connective tissue membrane, which appears to represent the inner layer of the pia. Both these layers are lost posteriorly in the subcutaneous connective tissue layer already mentioned.

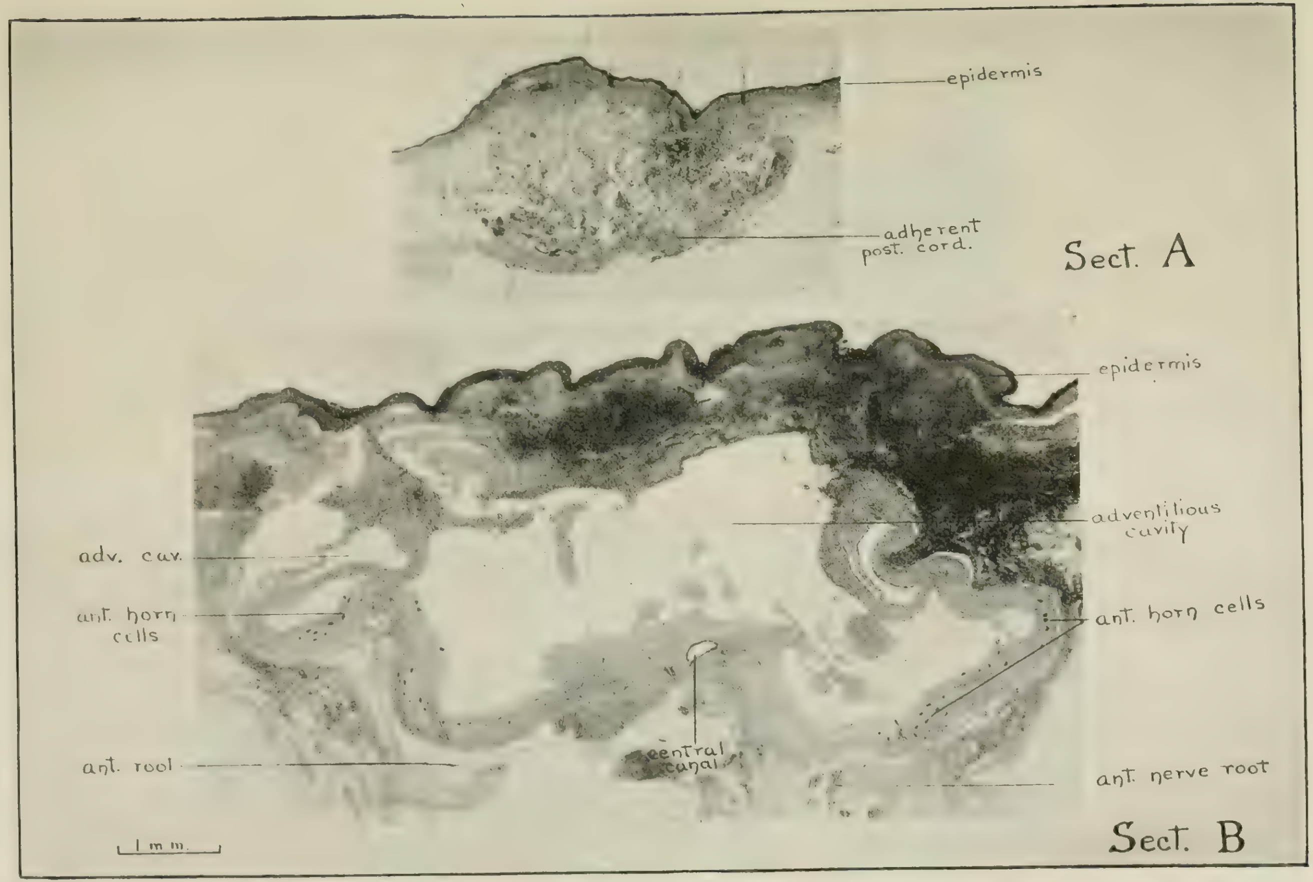

FIG. 15.—Case IV, lumbo-sacral cystic myelocele. Photomicrographs of Sections A and B at the levels indicated in fig. 14.

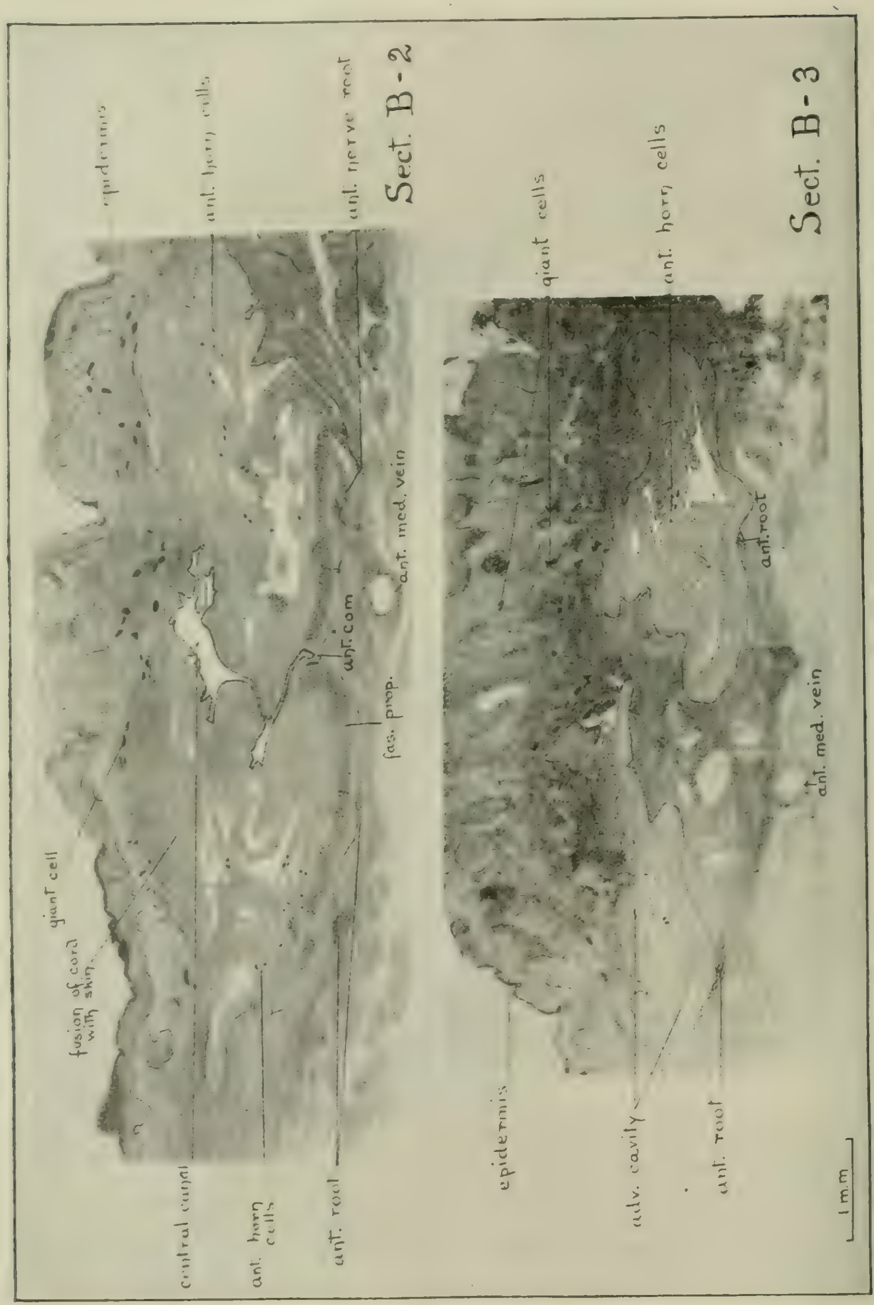

FIG. 16.—Case IV, lumbo sacral cystic myelocele. Photomicrographs of Sections B-2 and B-3 at the levels indicated in fig. 14.

The most striking feature in the cord is a large, irregularly-shaped fluid-filled cavity, which in the section is much distorted by the operative procedure. This is not a dilated central canal; it is not lined by any membrane, but by the neuroglia of cord substance. Posteriorly on each side is a smaller cavity, separate from the main cyst, which in the light of observations on other cases may possibly represent the position of undeveloped posterior columns. No trace of the posterior horns or columns can be found, but there is an irregular mass of neuroglia on each side. Toward the mid-line these masses are lacking, and the cavity in the cord tissue is bounded by the subcutaneous connective tissue layer. Anteriorly there is a well-formed, ependyma-lined central canal, and on either side of this well-formed anterior horn cells can be found, irregularly grouped along the anterior wall of the cystic cavity. Myelinated fibres are seen to pass from these and to emerge as fairly large anterior nerve roots. There are also numerous myelinated fibres forming a marginal zone over all the anterior half of the cord; these are probably all association fibres.

In the connective tissue surrounding the cord the nerve bundles are found arranged in two groups; one of these lies anterior to the cord in the mid-line, and then passes outwards to the sac wall. Into this group the anterior root fibres may be seen to pass from the cord. The other group lies close to the surface epithelium, and none of the fasciculi can be traced to the cord. It appears that the fibres in this second group represent the posterior roots approaching the cord from the spinal ganglia, but they never reach it, otherwise some should have been found in the great number of sections examined. This presupposes the proper development of the spinal ganglia, which is not owing to the circumstances of the case capable of proof. As has been seen, however, in the discussion of Cases I and II, the spinal ganglia sometimes develop even in cases with more marked neural tube defects than are here present, and the relationships of these fibres placed posteriorly to ligamentum denticulatum, makes it reasonably certain that they represent posterior roots. Between Sections B and C the cyst rapidly narrows. Microscopically the small central canal which is present in Section B enlarges posteriorly, and gradually assumes the proportions seen in the next section. It does not, however, communicate with the adventitious posterior cavity, but extends dorsally until it comes in contact with the subcuticular fibrous layer, and thus separates the adventitious cavity into two.

Section B-2.—Three millimetres below Section B (fig. 16—B-2). The most striking feature of this section is the huge central cavity which abuts directly against the subcuticular fibrous layer without the intervention of any nervous tissue. Its ependyma is unbroken, and the irregularity of shape is due to collapse of the wall in preparation. On either side the adventitious cavity seen in Section B is similarly collapsed and is broken up into smaller compartments. The anterior median fissure is shallow, and the anterior commissure hardly discernible. Anterior horn cells are still present but are few in number. There are a few myelinated fibres in relation to the anterior horn cells and in the region of the antero-lateral fasciculus proprius, but the anterior roots, which are found in the region indicated in the photograph, are largely non-myelinated. All the rest of the nervous tissue is composed of undifferentiated glia and possibly unmyelinated fibres.

In the following sections of the series the central canal becomes smaller, first anteriorly, and in lower sections posteriorly also, and the anterior median fibrous septum passes more and more dorsally until at the point where the central canal disappears entirely the nervous tissue is separated into two halves by the fusion of the anterior median septum with the fibrous subcuticular layer.

Section B-3.—Two millimetres below Section B (fig. 16—B-3). In this section one or two anterior horn cells may still be found. The nervous tissue is separated into two masses by a thick septum of fibrous tissue which extends dorsally to the subcutaneous tissue; in each of these irregular adventitious cavities are present, the continuation of those seen in higher sections. One or two anterior horn cells are present; but the remainder of the nervous masses, composed of glia and possibly unmyelinated fibres, can hardly be recognized as cord tissue. Between the surface epithelium, which is partly destroyed in the median line by ulceration, and the nervous tissue, a small number of giant cells are present and a few irregular epithelial strands.

Distal to this section the nervous masses become more and more indistinct, and about one millimetre below this level the appearance is exactly similar to that in Section C, though this is taken at a lower plane.

Section C (not photographed).—Through the median band, 11 mm. below Section B (fig. 14), 6 mm. below Section B-3. Laterally the character of the surface epithelium, connective tissue and meningeal layers is precisely like that in Section A. In the middle 10 mm. of the section, however, the surface epithelial layer loses its stratification, and merges into a mass of ulcerated imperfectly differentiated epithelium of considerable thickness, which is ulcerated and forms the bulk of the section in this region. Many small blood-vessels course through this mass, and its deeper layers are crossed by transverse bundles of fibrous tissue. Deeper down it is rather sharply limited by a connective tissue layer corresponding in appearance with the pial layer in the preceding sections. Between this and the more superficial connective tissue are irregular masses of epithelium of embryonal appearance, some of which are clearly neuro-epithelium.

Scattered through the epithelial masses are many irregularly shaped giant cells, such as are found in the two preceding sections. Some are of great size, and contain large numbers of irregularly disposed nuclei. They do not conform to the type of the usual foreign body giant cell, and are difficult to explain. None are found beneath the pia. Probably they are endothelial in origin and may represent imperfect budding capillaries. The elongation of some of the larger cells, and the presence of red blood cells in one or two, seem to bear this out.

Section D (not photographed).—This section is taken 14 mm. below Section C, at a point where the thickened median band begins to thin out near the end of the sac. It shows the surface and meningeal layers already described in Section A, and is of interest only because of the absence of the giant cells seen in the last section, and because laterally it possesses medullated nerve fibres, though it contains no cord elements. These are the posterior roots described and shown in fig. 14. The examination of sections between this and Section C shows that they do not pass up to the well-formed cord above, but are lost in the fibrous tissue.

Case V.

Hydromyelo-cystocele—rachischisis completa restricta of Class 3, A.

Specimen No. 77, University of Texas Pathological Museum (1893).

History.—The baby had been admitted to hospital at the age of 1 year for treatment of a lumbo-sacral meningocele. Following the injection of Morton's fluid, then in use (1893), the baby promptly died. No facts regarding muscular power are available; the baby had double congenital talipes equino-varus.

Description of specimen (fig. 17).—All the lumbar and sacral vertebræ had been removed with the tumour, bisected along the mid-ventral line and spread apart so as to expose the cord and the floor of the tumour from in front. Posteriorly the greater part of the right wall of the meningeal sac has been dissected away so as to expose its interior.

The upper three lumbar vertebræ are normal; the spine of the fourth lumbar vertebra is slightly smaller than normal: the fifth lumbar is cleft, its laminæ and spines flaring outwards. The columns of the sacro-spinalis muscle spread outward also so as to obtain attachment to the flaring spines. All the sacral vertebræ are bifid; but while the spines of the upper three flare, those of the last two are not more widely separated than in the normal sacrum. Through the opening in the spinal canal, the meninges and cord pass dorsalward. The meninges are adherent to skin and form a large sac, to the middle of which the cord is attached. It measures 4 cm. in antero-posterior and 3½ cm. in vertical diameter, but shows evidence of shrinkage during fixation. The skin covering it is fairly thick and has the appearance of normal integument, but section shows that it is without a fatty layer, and that its inner surface is inseparably fused with the dural layer of the sac. The further study of the sac will be simplified by reference to the drawing (fig. 17) which was made from the specimen and reproduces as nearly as possible the results of dissection. The only feature in which it is diagrammatic is that the cord is represented in longitudinal section throughout the whole of its upper portion, and the central canal as greatly enlarged. This was not visible to the naked eye in the dissection because of the collapse of the walls of the cord from the point B in the drawing, to the upper end of the cord in the normal canal; the dilatation is, however, easily demonstrable in sections at various levels. This will be more fully explained later.

Under the fourth lumbar arch the cord passes dorsalward at a sharp angle to the roof of the sac, where it flattens out and adheres to the middle of its roof. Above its point of attachment a fairly strong connective tissue septum extends downward from the sac roof to the lateral surface of the cord, where it blends with the pia. Where the cord passes into the normal canal above, i.e., at the "neck" of the sac, this septum is very narrow and fuses on the ventral side with the pia around the cord and on the other with the dura mater of the sac wall. In the dissection only the left side of the cord shows this septum, but along its right aspect there is evidence that a similar septum had been cut away, and that in the original condition the cord was slung between these two. On examining the posterior portion of the cord between the septa, it is found to be degenerated and to bear no posterior root fibres. Where the cord emerges from the canal and enters the sac nerve roots may be seen to pass from its posterior surface and to blend with the upper part of the roof of the sac as shown in the diagram. The anterior surface of the cord appears to be normal and its nerve roots pass out

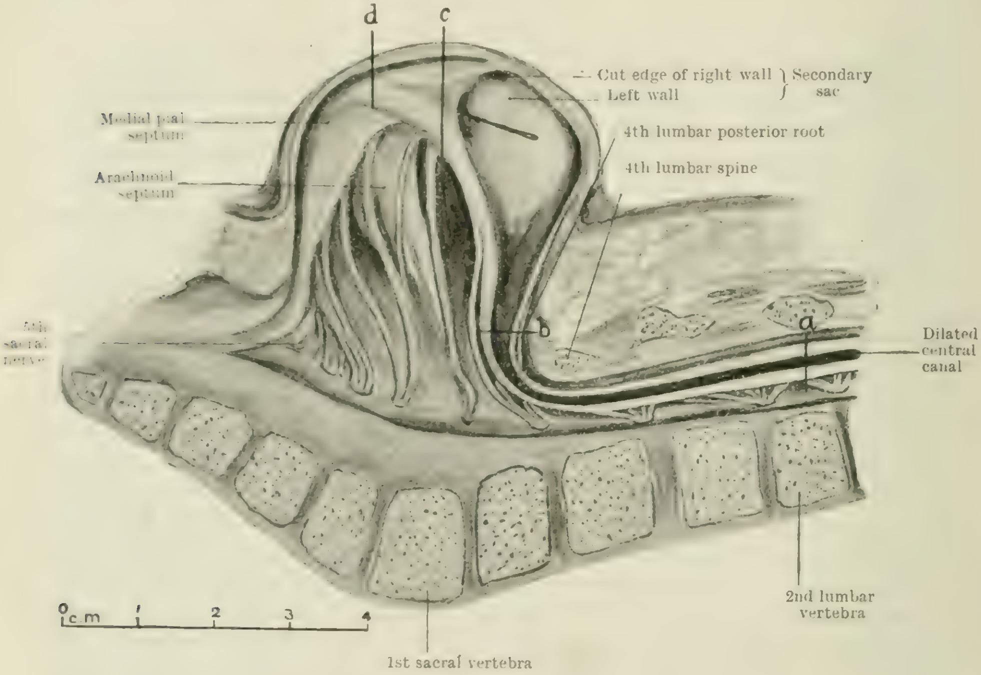

FIG. 17.—Case V, lumbo-sacral cystic hydromyelocele. Longitudinal section through sac as removed at autopsy. Cord had collapsed as result of a fixation from the point b upwards, and is represented in its dilated condition. In all other respects the drawing accurately reproduces the condition of the preserved specimen. A probe is passed into the right lateral pocket of the dilated cord cavity. Levels of microscopical sections indicated by letters a, b, c, d.

and course forwards toward their foramina. It seemed probable from the dissection that the septa just described had enclosed within them the dilated posterior part of the cord, and further study proved this to be the case. The preservation of the sac wall had not been sufficiently good for any nervous elements to remain uninjured in the exposed region where the right septum had been dissected away. It is found, however, that where the end of the cord joins the sac wall it is much flattened and that the secondary sac just described passes into two lateral pockets. One of these, the right, is shown in the drawing with a probe passing into its depths. These pockets terminate close to the lateral masses of the cord tissue below, and, as will be seen later, they are lined by ependymal cells. Moreover, at the point B in the diagram, where the cord in the preserved specimen is small and flattened, section shows that its walls are thin and fluted, indicating that it had been greatly distended with fluid. Higher up in the normal canal the cord appears flattened in an antero-posterior direction, and here also gross and microscopic section shows that there has been collapse of a large interior cavity. This and other microscopical observations prove that the secondary sac consists of a cyst of the dorsal part of the cord, surrounded by pia and adherent to the sac surface, and it is so represented in the diagram.

Distal to the attachment of the cord, another delicate septum extends like a veil about half way through the depths of the sac, and laterally on the left side (the right side has been dissected away) is another septum which terminates higher in the sac wall. The relationships of the nerve-roots to these septa show that the medial veil is pial and the lateral is arachnoid.

As is shown in the drawing, the lower part of the sac is traversed by many nerve-roots. These lie medial to the arachnoid septum and lateral to the pial septum mentioned, and are more or less entangled in delicate fibrous trabeculæ, which bind them to the sac wall. The last roots which emerge from the well-formed cord, before its attachment to the sac roof, are the fifth lumbar roots, and of these the anterior radicles come from the cord, and the posterior roots from the sac wall where it is adherent to the posterior cystic cord. The roots below these are fairly large, but not so large as those in a normal fœtus at term. They are divided into two groups, anterior and posterior, which unite in the usual manner and pass into foramina in the floor of the sac. They do not, however, appear to join any normal cord tissue on the roof of the sac, but to come directly from the sac wall at a point below the demonstrable cord. It was not possible to dissect these after they became adherent to the roof of the sac, as they are fused with the dense tissue of its dural lining.

The arrangement of the roots above the lesion is, perhaps, sufficiently clear from a study of the diagram alone, since it is in no way different in principle from that found in Cases III and IV, of which full explanation was given.

Microscopical examination (figs. 18 and 19).—Sections were made at the levels indicated in fig. 17. In spite of the age of the specimen the staining with iron-hæmatoxylin was very satisfactory, though the other stains were not successful. The only serious difficulty was that the tissues were so friable that it was difficult to cut blocks for examination without tearing the sections. This was especially true of the dilated cord as it entered the sac. In the removal of the right myelocele wall the pia had been incised, and when Section B was cut its walls spread into a long thin ribbon of tissue, and lost their circular conformation. The examination of the sections was, as a whole, much more instructive than one would expect after so long a time in preservatives.

Section A (fig. 18).—Level of the second lumbar vertebra, above the lesion. The foramina through which the nerve-roots pass indicate that this is the first lumbar segment of the cord. The shape of the section is flat, as the result of the escape of fluid from its interior, owing to tearing of the pia. The anterior median fissure is normal; in the posterior median line a small fibrous septum composed of pia extends inwards almost to the central canal, from which it is separated by a glial commissure connecting the two halves of the cord. In sections at the upper part of this block of tissue, 1 mm. above the section photographed, this adventitious pial septum disappears, and the posterior glial septum is normal. It therefore represents the beginning of the abnormal adherence between the posterior wall of cord and the meninges, which is so much more intimate lower down. The central canal is very large and flattened antero-posteriorly, due to the escape of fluid. Anterior horn cells are well formed though few in number, but it must be remembered that the cord was pulled out by traction from the sac below, so that the cells in a given section would be less numerous than when the tissue was normally concentrated; and the total number of cells in each segment is not necessarily reduced. In certain of the sections from this area anterior nerve-roots emerge in the region indicated in the photograph. Posterior horn cells cannot be distinguished; the position of entering posterior root fibres is shown. Myelinated posterior columns are present, and there appears to be a small lateral cerebrospinal tract and a number of other myelinated fibres, some of which may represent descending tracts. They are not sufficiently well differentiated to name them with accuracy; probably many belong to the fasciculi proprii. The median part of the posterior column, usually occupied by the long fibres from the posterior roots, contains less myelinated fibres than the lateral part. This part is composed of the lower of the ascending posterior root fibres, and in this specimen many of these are caught in the meningeal sac and never reach the cord. Throughout the section there is a preponderance of glia cells and a considerable number of lymphocytes.

Section B (fig. 18, B):—Dilated cord just below its entrance into the sac. The nerve roots which originate here pass into the fourth lumbar foramina, so that this represents the fourth lumbar cord segment. The cord here was contracted into a flat, narrow band, but when the section was cut it stretched widely, so that it was evident that it had been greatly distended with fluid. The attempt to preserve its circular form was a failure and the photograph shows only a small portion of the anterior region. The pia over all the section is thickened, and posteriorly it blends with a dense dura-arachnoid, the layers

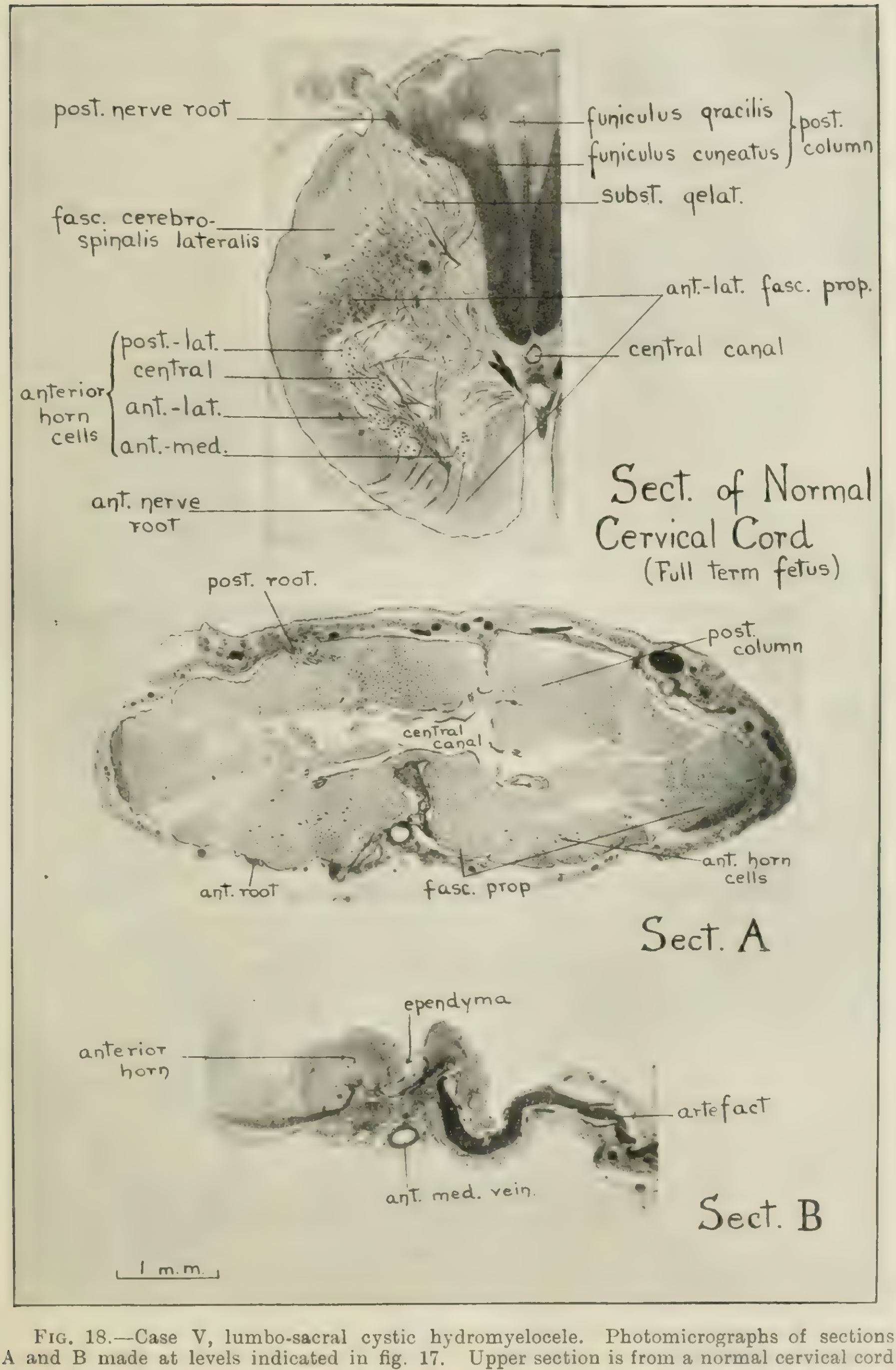

FIG. 18.—Case V, lumbo-sacral cystic hydromyelocele. Photomicrographs of sections A and B made at levels indicated in fig. 17. Upper section is from a normal cervical cord of a full term fœtus for comparison, under the same magnification as other photographs.

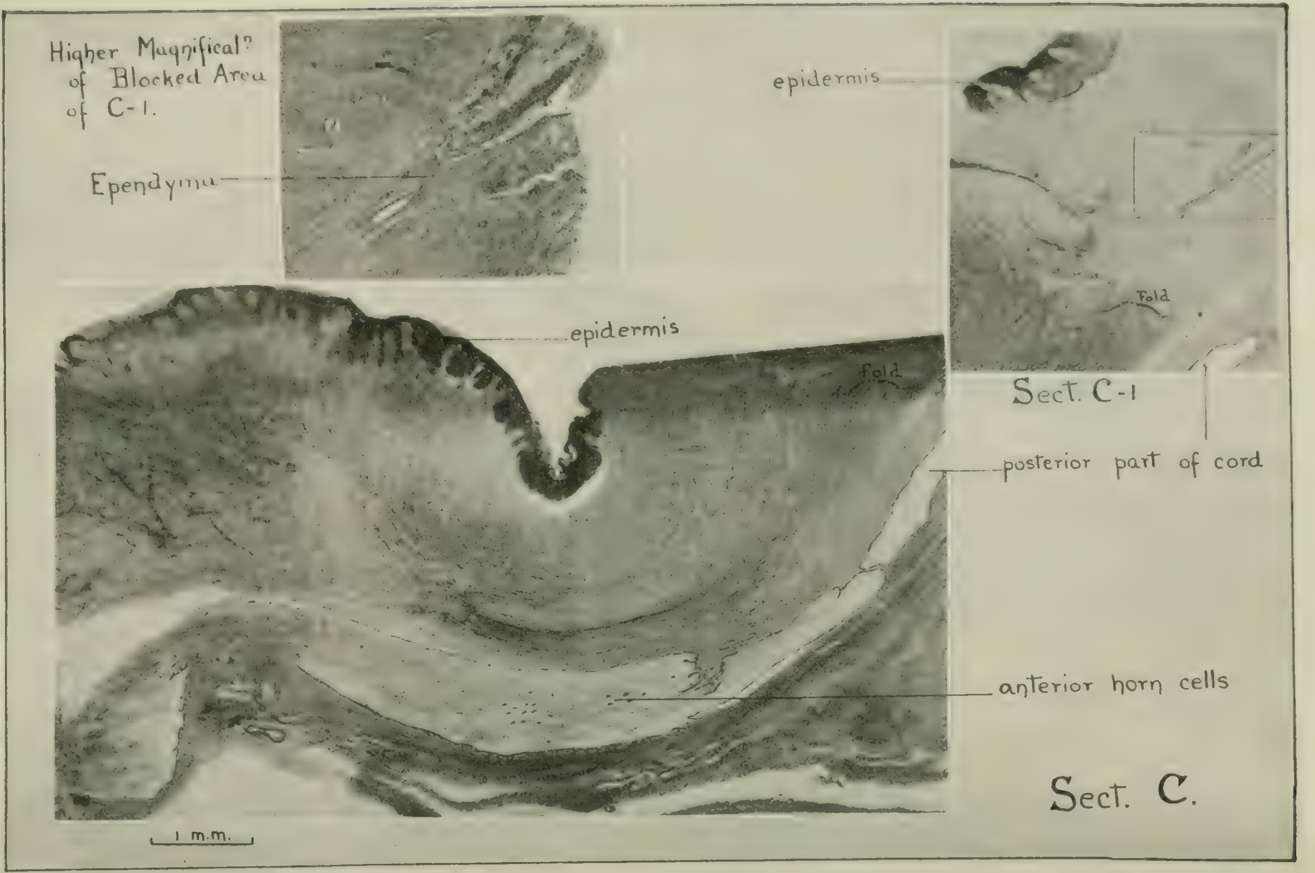

FIG. 19.—Case V, lumbo-sacral cystic hydromyelocele. Photomicrographs of Section C, made at level indicated in fig. 17. Section C-1, from the lateral pocket. Fold in section coincides with that in Section C.

of which are indistinguishable and infiltrated with inflammatory cells. This dural layer blends posteriorly with the subcutaneous fat in the neck of the meningocele. The anterior mid-line is indicated by a short prolongation of the pial layer inward and a large anterior median vein, but there is no true anterior median septum. Near this many bundles of myelinated nerve fibres (anterior roots) are found lying in the pia where it blends with the dura of the sac. Emerging anterior root fibres are found near the median line, but posterior roots could not be seen entering the cord. Within the pia there is a small layer of nervous tissue. This is somewhat thicker near the anterior median line, and in this region there is a diverticulum from the general cavity which appears to be imperfectly lined by ependymal cells. On either side of the median line there are a number of vacuolated cells with pale nuclei, which possibly may be anterior horn cells which have undergone degenerative changes. No other nerve-cells are present; the layer of tissue is an indiscriminate mixture of partly myelinated fibres and neuroglia with a few small vessels and occasional lymphocytes, but with no landmarks by which one can recognize even its regions with accuracy. Except for the few doubtful ependymal cells mentioned above the central cavity is without definite lining, and is bounded by the degenerated nervous mass which has been described. It is impossible from this section, therefore, to say whether the cyst is a dilated central canal or an adventitious cavity, though it seems probable from the sections above and below that it is a dilatation of the central canal.

Section C (fig. 19, C).—Wall of sac and attached end of the cord, with the lateral pocket of the hydro-myelocele. The nerve-roots from this portion of the cord are those of the first sacral nerve, indicating that this represents the first sacral segment of the cord.

The surface epithelium is fairly thick and has a few papillary processes; hair follicles and skin glands are lacking, as is the subcutaneous fatty layer. Beneath the epithelium are dense bands of fibrous tissue, the fibres of which run transversely to the long axis of the cord. Below this fibrous layer is a layer of looser, more delicate connective tissue, considerably infiltrated with round and polynuclear cells. Laterally this layer extends about 5 mm. from the middle line, and there splits into two leaves, of which one passes laterally to merge with the dura-arachnoid lining of the sac. The other passes medially, and with the corresponding leaf of the opposite side forms a sheath for the attached end of the cord. The whole of this layer, which represents pia, is densely infiltrated with inflammatory cells. At the middle line the anterior layers project upwards towards the roof of the sac, forming an imperfect anterior median fissure in which the pia is distinguished by its great vascularity. The cord tissue enclosed between the layers of this pial sheath bears little resemblance to normal cord. The inflammatory connective tissue which bridges the gap between anterior median septum and sac roof divides the nervous tissue into two masses; no nervous elements can be recognized connecting these across the median line. No trace of central canal is present. In each lateral nervous mass certain nervous structures can be determined. The photograph (fig. 19, C) shows but one lateral half and a very small portion of the other, with the median anterior septal mass of connective tissue already described. It will be seen that the cord is not rounded, but is represented by a flattened band, each half of which is roughly divided into two regions. In the more medial of these anterior horn cells normal in size and shape are easily recognized. Lying between them are many glia cells, and many fibroblasts and inflammatory cells. In the more lateral of the nervous masses no nerve cells can be distinguished, the mass consisting of glia infiltrated with a few inflammatory cells. No myelinated fibres can be found in any portion of the cord tissue, save one or two delicate scattered fibres in the region of the anterior horn cells. In certain of the sections from this region anterior root fibres emerge in the position indicated in the photograph. No posterior root fibres can be found entering the cord tissue.

Passing laterally to the outer limit of the posterior region of the cord (i.e., the lateral glial masses), separated from these by the fused dura-arachnoid lining the interior of the sac, and lying near the integumentary epithelium but separated from it by connective tissue, is the lateral pocket of the dilated proximal portion of cord. (Cf. fig. 17, in which a probe is passed into this pocket, and the description of the gross findings.) This pocket is shown in C-1 on fig. 19. It is lined with a perfect layer of ependymal cells, surrounded by a narrow zone of glial cells, among which there are a few myelinated fibres. In the more distal sections from this block the pocket ends blindly in a small glial mass ; it never makes any direct connection with the lateral cord masses at this level. As one passes caudalwards from the end of the cord the sections show the same general characteristics, but the anterior horn mass becomes less definite, and the lateral (posterior) masses are separated into smaller portions by strands of connective tissue. They spread also more laterally, and 2 mm. distal to the section shown in the photograph are so attenuated and mingled with connective tissue that little neural character remains.

Section D (not photographed).—Taken 5 mm. below the level of the block cut for Section C, through the wall of the sac where cord tissue has apparently blended with it.

Here there are a few imperfect hair follicles and sweat glands ; no subcutaneous fat is present. The tissue below the epithelial layer is denser connective tissue than is normal, and towards the interior of the sac it blends with the dura arachnoid and with an imperfectly differentiated pia, between the layers of which are nerve bundles. These are numerous and conspicuous, but examination shows that they contain but few myelinated fibres lying between connective tissue and inflammatory cells. The apparent large size of the nerve roots seen by the naked eye is therefore misleading. A small glial mass is found at the median line, but this contains no true nerve cells nor central canal. The surface epithelium immediately above this glial mass shows an unusually deep slender papillary process of elongated spindle-shaped cells ; but no connection between this and the glial cord mass can be demonstrated, as they are separated by bundles of connective tissue.

General Discussion of Cases III, IV, and V.

The points of interest in these three cases are discussed together because clinically and anatomically they are closely allied.

(1) The lesion in all is lumbo-sacral and had the clinical appearance of a pure meningocele, though in two of the cases ulceration of the sac wall might have led to a suspicion of involvement of the cord.

(2) In each the cord is bound to the wall of the sac by the segment corresponding to the highest vertebral segment which is cleft.

(3) The collection of fluid has drawn the cord above the proximal affected segment down into the sac, so that higher segments are influenced by traction.

(4) Hydromyelia in cord segments above the lesion is present in each case, extending as high up as the cord was removed at autopsy in two cases and as high as it could be observed at operation in the case without autopsy, and for an unknown distance above this. In Case V this is most marked and is complicated by the adherence of the intrasaccular portion of the cord to the sac wall, causing a secondary myelocystocele.

(5) The cord at the level of the point of attachment in each case is cut off from both ascending and descending nervous connections by the adherence of cord tissue and nerve roots to the sac wall, so that even before operative interference the lesion amounted to an almost complete transverse lesion of the cord at this point.

(6) Segments of the cord lying distal to the segment attached to the sac are imperfectly developed and partly destroyed by the adherence to sac wall; and there is evidence to show that they have never been closed but represent a persistent neural groove which has been overgrown by adhesions and integument.

In Case IV this is capable of direct proof, as is shown in fig. 14, Section C, where partly differentiated epithelium of mixed neural and integumentary character is found on its external surface. In Cases III and V the overgrowth of skin epithelium has obscured the defect to a greater extent, but the lateral spreading of the nervous tissue, the absence of central canal and the position of nerve-roots with reference to the ribbon-like band of cord tissue, indicate that in these cases also the initial lesion has been a failure of closure of the lower sacral segments. Later, the meningeal layers have grown over the defective cord, and to a less marked extent over the open medullary ribbon in Cases I and II; and still later the skin epithelium has covered the whole, and the adhesions so formed have destroyed any vestiges of ependymal cells which may have been present. It has already been noted that in complete lesions involving the whole of the neural tube (Case II) there is a tendency for skin to grow over the lower part of the defective area; the tendency of the skin epithelium even in the adult body toward growth is clearly shown in all granulating superficial wounds.

The accumulation of fluid in the meningeal part of the sac is always in these cases a secondary occurrence, and accounts for the dragging of the normal cord outwards. The accumulation of fluid in the cord tissue itself is a result of its abnormal adhesion. No satisfactory explanation of the collection of fluid in either the meningeal or the medullary sacs has yet been given. It cannot be even suggested from a study of these cases alone, but involves the consideration of the whole subject of the normal production and absorption of cerebrospinal fluid and all the possible abnormalities thereof.

CASE VI.

Myelocele rachischisis completa restricta of Class 3, A.

Specimen No. 802, University of Texas Pathological Museum.

The specimen is of a full-term white female, length 38·5 cm. from vertex to coccyx. The external appearance is normal except for a considerable degree of hydrocephalus and a lumbo-sacral spina bifida. The head had been lacerated to promote delivery, and there are forceps marks upon the thighs. The body is somewhat degenerated, but there is no evidence that death had occurred before the beginning of labour. The degeneration appears to be the result of imperfect preservation, as the body had evidently been allowed to dry, and then had been placed whole in fixing fluid without any injection. For this reason the examination is in some respects unsatisfactory.

Dissection.—The head measures 49 cm. in circumference, but there has been some collapse which cannot be accurately estimated. The brain has been entirely destroyed by stuffing the cranial cavity with cotton, so that only a small irregular mass of tissue remains at the base, which cannot be identified by the naked eye, and its preservation is such that microscopical sections are of no value. The exposure of the vertebræ from behind shows that all the cervical, all the thoracic, and the first three lumbar vertebræ are normal. The laminæ of the fourth lumbar meet in the median line, where they are fused by a cartilaginous union, but they do not possess any spinous processes. The laminæ of the fifth lumbar are directed towards the median line, but are separated from each other by a space of 7 mm., which is bridged by a band of connective tissue. The sacral laminæ flare outward, and are somewhat smaller than normal. The coccyx appears to be normal.

These lower vertebræ from the fifth lumbar to the last sacral are covered externally by the parchment skin of the myelocele, of which the external appearance is shown in fig. 20, B. It will be described in detail later.

Dissection of the spinal cord and meninges above the level of the fifth lumbar vertebra shows that the meningeal layers are normal, but the dural sheath is somewhat collapsed, the epidural space being occupied by a gelatinous exudate, and the vascular and fatty tissue normally found here is reduced in quantity. The spinal ganglia are normal in size and position in all this region of the cord, but the dural sheaths of the spinal nerve roots, which should incline very slightly caudalward in the lower thoracic and lumbar areas, have a transverse direction. On opening the dura-arachnoid the cord is found to be soft and poorly preserved, so that only with great care in handling can the nerve roots be traced. Those roots from the cervical and upper ten thoracic segments are normal in direction (cf. fig. 5, B), the tenth thoracic roots arising from the cord at the level of the body of the ninth thoracic vertebra. From this point they tend to lose their downward inclination, and present the relationships shown in fig. 20, A, that is the eleventh thoracic roots arise from the cord at the level of the tenth vertebral body; the twelfth thoracic roots from that at the level of the eleventh and twelfth vertebræ; the first lumbar roots from the cord at the level of the first lumbar vertebra: the second lumbar from the cord at the level of the second and third lumbar vertebræ; and the third lumbar roots from the level of the third and fourth lumbar vertebræ. The fourth and fifth will be considered in the description of the

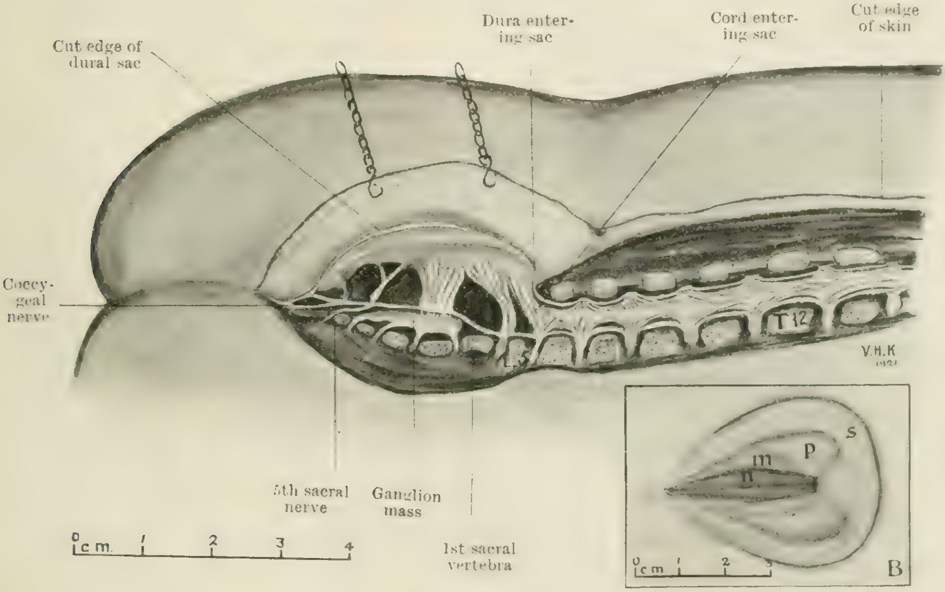

FIG. 20.—Case VI, lumbo-sacral myelocele. Dissection of right side of myelocele. B, external appearance.

myelocele. The condition of the cord is not such that any further examination can be made: it appears to be considerably smaller than normal, but definite evidence of collapse of a cystic condition remained.

Myelocele.—The parchment skin of the myelocele is somewhat wrinkled but flat, and there is no sign of a previous distension with fluid. It measures 35 mm. in transverse and 45 mm. in vertical diameter, and extends from the level of the fifth lumbar vertebra to that of the fourth sacral. At the level of the fifth sacral in the median line the skin is normal; a small tuft of fine hair is present here, but this is no more than is frequently found in this region in normal infants. The character of the wall of the myelocele is of considerable interest. As is seen in the drawing (fig. 20, B), it is pyriform with the apex directed caudalward. The upper part is rather sharply marked off from the surrounding skin by a groove, which disappears in the lower third of the "pear." Within this for a distance of 12 mm. at the broad end, and 10 mm. at the narrow end of the sac, the skin (s) is normal in appearance, except that it is slightly elevated above the level of the surrounding skin. Within this there is an irregular zone of wrinkled parchment skin, delicate in texture, without fatty layer; under a hand lens it shows fine hair and pores. At the upper part of the sac this zone (p) is blended with a very narrow zone of membrane (m), without evidence of epithelial covering, i.e., a meningeal layer; but at the lower part there is no such zone. Down the mid-line of the sac lies a band of brown tissue (n) which has the appearance of being covered by dried blood. This merges above and below into the skin surface of the peripheral zone of the sac, but laterally it is fused with the meningeal zone. The specimen had become dry before it was placed in preserving fluid, for this band of tissue, which is obviously the medullary groove, is contracted and hard, but there is no degeneration of this region which interferes with the dissection of the lesion.

Dissection (fig. 20).—The myelocele was surrounded by a circular incision and the skin surrounding it dissected up with its subcutaneous layer and turned towards the median line. At the inner margin of the peripheral zone of the skin (fig. 20, B) the subcutaneous fatty layer disappears and a meningeal sac is found. The limits of this correspond very closely with the outer border of the flaring sacral laminæ, but caudally it extends no lower than the fourth sacral vertebra. On cutting through the lateral margin of this and reflecting it, the dorsal wall of the sac is found to be composed of a fusion of dura and arachnoid with surface epithelium, and to pass medially into the medullary ribbon. The ventral wall is composed of dura and arachnoid, and lies in contact with the bodies and exposed dorsal surfaces of the flaring laminæ of the sacral vertebræ. In order to study the relationships of the medullary ribbon more carefully, the bridge of connective tissue arching the gap between the fifth lumbar verebral laminæ was dissected away and the pedicle of this vertebra cut to show the foramen for the fifth lumbar nerve. The flaring laminæ and spines of the sacrum were also removed, exposing the posterior sacral foramina.

At the level of the fifth lumbar vertebra the dural layer of the sac passes under the fibrous arch into the spinal canal. The opening in the dura was continued from the sac below to that already made in the sheath of the cord above, exposing the spinal cord as it passes from the canal into the upper part of the sac roof, where it becomes continuous with the medullary ribbon. In fig. 20 this dissection is shown on the right side. It will be seen in the drawing that the traction of the reflected area of the sac has pulled the cord and medullary ribbon out of the vertebral groove in which they lay, and the length of the closed part of the cord, from the neck of the sac to the roof, is somewhat exaggerated. The fourth lumbar nerve roots arise partly from the cord in relation to the fourth lumbar vertebra (above the sac) and partly from the closed cord as it passes under the fifth lumbar fibrous arch to the medullary ribbon. The fifth lumbar root arises from the proximal part of the medullary ribbon; its ganglion is normally situated. The roots of the upper four sacral nerves of the right side are grouped together so closely that no absolute differentiation between individual nerves, nor between anterior and posterior roots can be determined. This clump of fibres passes through the dural floor of the myelocele, and into an elongated mass of nervous tissue enclosed in a prolongation of the dural sheath, lying in the groove representing the open sacral canal. From this, nerves can be traced to the upper four posterior sacral foramina. It therefore represents the upper four sacral ganglia fused into one mass. Certain of the proximal radicles of this clump appear to pass medial to the ganglionic mass and directly into the anterior foramina, but the tissues are so delicate that this cannot be definitely proved without more destruction of the specimen than seems justifiable. From the medullary ribbon distal to the clump of roots described, two delicate roots, on one of which there is a small ganglionic mass lying *within* the dura, pass out as the fifth sacral nerve. Still more distally a delicate strand passes down from the ribbon; this probably represents the coccygeal nerve, though it is too delicate to be definitely identified, and no ganglion could be found upon it. Distal to this the medullary ribbon, which has narrowed to a sharp point, passes into a slender fibrous strand and by this is connected with the dural floor of the myelocele, and through this to the coccyx and subcutaneous tissue over it.

On the left side the condition is similar except that the first sacral root has a normal ganglion, and anterior and posterior radicles can be differentiated; the ganglia of the second, third and fourth sacral are grouped into one mass, as on the right side. The fifth sacral has a well-developed ganglion occupying its normal position outside the spinal sheath of dura. It should be mentioned that there is some doubt as to the ganglionic character of the intradural mass on the right fifth sacral. It is much smaller than normal, and indeed the roots on this side are much smaller than the corresponding roots on the left side; and very close to the medullary ribbon. There was no other ganglion on this nerve-root; for various reasons no section of this minute body was made.

Microscopical examination.—An attempt to procure material for examination of the cord above the lesion was an absolute failure. The tissue was so degenerated that nothing could be done with it. The tissue of the myelocele was hard but well preserved, as was the ganglionic mass. The sections were taken from the fifth lumbar and first sacral segments (fig. 20). It seemed best not to destroy the specimen for museum purposes and therefore no serial sections were made below this level.

Section A (fig. 21, A).—Just below the attachment of the cord to the roof of the myelocele, representing the level of the first sacral segment of the cord. On the right side the skin surface shows many sweat glands and numerous small hair follicles which are more deeply situated than normally. This zone of skin is that marked "n" in fig. 20, B. It passes rather suddenly into a fibrous layer "m," apparently meningeal, but covered by a thin layer of stratified squamous epithelium which has no papillæ nor other integumentary structures. This zone in turn passes medially and the fibrous layers are fused with the pia which lies ventral to the ribbon cord. The layer of surface epithelium ends rather abruptly on this side of the specimen in a mass of epithelial and blood cells which separates it from the outlying (posterior) portion of the ribbon cord. One small mass of glia is found in the fibrous tissue just lateral to this hæmorrhagic area, and is covered by the surface epithelial layer. On the opposite (left) side the relations are somewhat different. The surface epithelium passes medially over the outlying area of ribbon cord and there terminates abruptly, and lateral glial masses of considerable size are found beneath the epidermis, separated from it by a thin layer of fibrous tissue which apparently represents corium. Non-myelinated posterior nerve-roots approach the glial masses on each side; on the right they are situated just beneath the hæmorrhagic zone; on the left, they appear to enter the cord where the surface epithelium terminates.

The structure of the medullary ribbon does not differ materially from that of the ribbon cord in Case I. Anterior horn cells are well developed; anterior nerve-roots are present but are not myelinated. At the middle line there is a depression corresponding with the central canal, and beneath it a narrow anterior commissure. This depression and the surface of the ribbon contiguous to it are covered by ependymal cells. The anterior white matter lies median to the spreading anterior grey horns. All of this region of the medullary ribbon is œdematous, and there are great numbers of small blood-vessels coursing through it. The majority of these are in definite trabeculæ of connective tissue. Laterally there remains but little evidence of the posterior portion of the cord, except the glial masses already noted as lying lateral to and separated from the main medullary tissue. The small posterior portion not separated from the main ribbon appears to be made up of glia and possibly nerve-fibres without any evidence of posterior horn cells. There are no myelinated fibres anywhere in the section.

The sections 2 mm. caudal to this show no great change except the gradual decrease in the number of anterior horn cells and the increase in the vascular invasion of the cord structure. The isolated glial masses noted

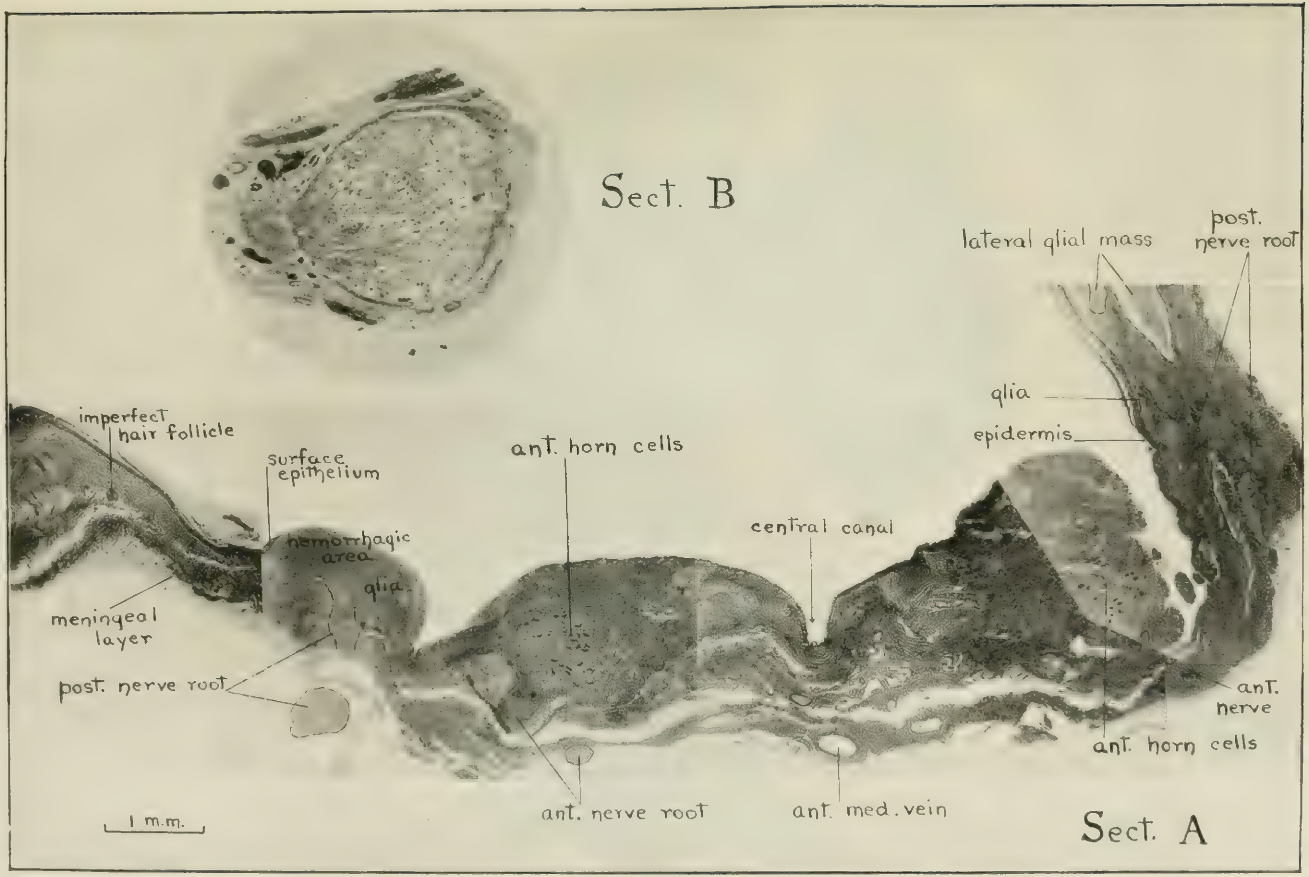

FIG. 21.—Case VI, lumbo-sacral myelocele. Photomicrograph of section through upper part of myelocele. B, section through fused spinal ganglion.

in the higher sections disappear in the fibrous tissue. The posterior portion of cord is therefore represented only by the small parts of the ribbon cord lying lateral to the motor cell group.

Section B (figs. 20 and 21, B).—Section of the fused ganglionic mass. The structure of this mass is typical and confirms the naked-eye observation that it represents fused root ganglia. It is abnormal only in the fact that the nerve-fibres are non-myelinated.

DISCUSSION OF CASE VI.

This case corresponds in many features with the preceding cases of restricted lesion, and throws light on certain obscure points in the interpretation of these.

(1) The cord is bound to the roof of the sac by the segment corresponding to the highest vertebra that is cleft.

(2) There is no excess of fluid in the myelocele or meninges, and the direction of the nerve roots above the lesion, therefore, is influenced only by the attachment of the cord; they pass to their foramina at right angles to the long axis of the cord.

(3) Hydromyelia and hydrocephalus are associated, indicating defective development of the entire medullary tube.

(4) The neural ectoderm of the involved segments, which is spread open in the form of a groove, is partially covered by epidermis and by connective tissue, so that the lateral part, which represents the posterior part of the cord, is to some extent separated into isolated neuro-epithelial masses. The overgrowth has not progressed farther than the outskirts of the ribbon, so that the original groove is plainly discernible. In the event of this overgrowth extending farther towards the median line, however, the resulting condition would be entirely similar to that found in the preceding cases. There is in this case, therefore, very strong evidence supporting the belief that the band-like cord substance in Cases III, IV and V represents open cord segments, and that the failure of the medullary tube to close is the primary lesion in these restricted defects as in the more extensive.

(5) The spinal ganglia are affected by the medullary defect, since they form a fused mass in certain of the segments. The defect in their development has not, however, either caused or been caused by defect in the corresponding vertebral segments, since these are segmentally normal even though they are incompletely fused dorsally.

CASE VII.

Meningocele—rachischisis incompleta restricta of Class 1, B.

History.—D. M., female, aged 11 months, John Sealy Hospital.

No family history of deformity nor nervous lesion. Child is healthy and well-developed except for the presence of a lumbo-sacral tumour. Control of bladder and bowels appears to be normal. Baby presents a small congenital tumour covered by parchment skin, about 1½ in. in diameter, occupying the sacral region. It is tense, its surface is unbroken, and is slightly painful on pressure. Operation, by Dr. J. E. Thompson, September 18, 1918, ether anæsthesia. Transverse incision made above and below tumour, and outer parchment skin dissected up, opening the sac. Within the parchment sac two others were found, lying one inside the other, as represented in fig. 22. The wall of the second sac was very thick and shining, and was thought at the time of operation to represent dura; fluid withdrawn from this sac gave a positive "glucose reduction." The third sac also contained fluid, but this was not tested for reduction. It was thinner and had at its upper end a small mass of spinal cord tissue. This sac was typical pia, but slightly thicker than usual.

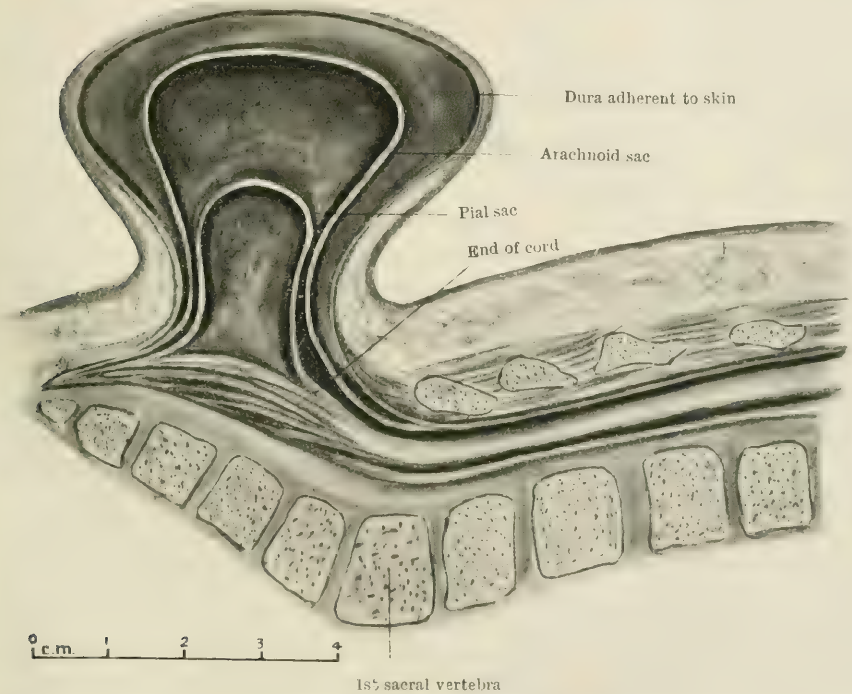

FIG. 22.—Case VII, meningocele. Posterior surface of cord shown as seen at operation. No facts available regarding nerve roots.

It was opened and its walls sutured over the *cord* (not cauda equina alone) which was found to lie inside it; the portion of cord lying in its proximal portion was not disturbed. The second sac, which was thought to be dural, was partly dissected away, and its edges sutured; and the parchment skin of the external sac was removed until normal skin was reached and this was finally sutured. Convalescence was ideal, and the baby was dismissed from the hospital, September 26. Later history: February, 1921, the mother reports that the child's general health is good and that she is bright mentally. She began to walk at the age of 18 months; at first she had a tendency to "turn the feet in," but this is improving. She has very good control of the bladder, but not of the bowels.

Discussion of case.—Unfortunately this case occurred before the writer's interest in spina bifida had been awakened, and the small portions of the meningeal sacs which had been dissected away in the operation were not preserved. The diagram shown in fig. 22 is reconstructed from a drawing of the sac layers made at the time of the operation. In the light of the conditions in other cases it is probable that the sac thought at operation to be dural was a thickened arachnoid sac, and that the inner sac was composed of the outer layer of the pia. The outer parchment skin was lined by a glistening membrane and filled with clear fluid, and this doubtless represented the fused integument and dura, as in other specimens described. The thickening of the arachnoid of the inner sac, which led to the misconception at the time of operation, is entirely in accordance with observations on Case IV, in which a partial transverse septum of arachnoid is found. The position of cord tissue in relation to the upper part of the innermost sac clearly indicates that this is pial. The drawing has been labelled according to this interpretation in preference to that made at the time of operation.

The feature of peculiar interest in this case is the presence of cord tissue in the floor of the upper part of this sac. The nervous tissue observed was spinal medulla and not the nerve roots of the cauda equina. It is obvious that no detailed examination of this nor of the cauda equina could be made. This much, however, was discovered, that the cord extended as far as the floor of the meningocele, i.e., as low down as the fifth lumbar vertebra, though it should end at the second. This indicates that in this case, in which apparently no structures except the meninges (mesoderm) were involved, there was at some time in the development adherence of ectoderm sufficient to bind the neural tube down in the vertebral canal. This is a feature of many of the "simple meningoceles" which has not received due consideration in the study of operative results, and accounts no doubt for the frequent lack of control of bladder and bowels in these patients.

GENERAL CONSIDERATIONS.

With a study of specific cases in mind, the review of the literature and especially the clinical literature can more readily appreciated.

For this reason all statistical and practical considerations have been deferred to this place. Neither time nor opportunity has sufficed for a complete study of all the available writings on the subject, yet it is hoped that this survey, in spite of its incompleteness, will not be without value. All matters which do not have a direct bearing on the anatomical study presented have been omitted.

Statistical Summary.

Frequency.—The Report of the Committee on Spina Bifida of the London Clinical Society, presented to the Society in 1885, cites the following frequency statistics: "Dr. Demme found 57 cases of spina bifida in 36,148 children; Chaussier records 22 cases among 22,293 children in the Paris Maternité." Harrar, in 1916, found 59 cases of spina bifida in 91,600 births in the Lying-in Hospital in New York. Grouping these figures we have an incidence of 1 in 900 births. Joseph gives the frequency of "spina bifida with tumour" as 1 in 1,000 births. Both these percentages omit the cases of spina bifida occulta, since these are not discoverable in the infant except in very rare cases. S. N. Clark gives the percentage of spina bifida occulta as 5 per cent. of all cases, but he evidently refers to cases giving rise to nervous symptoms. The mild varieties in which cleft of the laminæ or of the spines alone occurs without symptoms of pressure on the cord are fairly frequently encountered in the dissecting room. No facts regarding the percentage of all cases which are sufficiently limited to be of surgical importance are available.

Locality.—In 385 operative cases treated by excision, collected by J. E. Moore in 1905, the locality is given as follows: 23 per cent. sacral; 34 per cent. lumbar; 24 per cent. lumbo-sacral; 4½ per cent. thoracic; 9½ per cent. cervical; two cases were occipital. This represents the localization of the restricted (operable) variety of lesion only, but it is in such cases that locality is of practical importance.

Type of restricted lesions.—Unfortunately Moore does not give the percentages of different types of tumour encountered in his collection; doubtless in many of the cases he collected there was no specific information regarding this feature. Fenner places meningoceles at 10 per cent. and meningo-myeloceles at 70 per cent. to 80 per cent. of the cases. In a total of 170 cases in which accurate anatomical data are given, collected by the writer from the literature cited in the bibliography appended to this paper, the percentage is as follows: 7 cases (4·1 per cent.) spina bifida occulta (with symptoms); 4 cases (2·3 per cent.)

"meningoceles with adherent cauda equina"; 36 cases (21·1 per cent.) pure meningoceles; 120 cases (70·6 per cent.) myelo-meningoceles; and 3 cases (1·7 per cent.) syringo-myelo-meningoceles. As the meningoceles only in this series presented no nervous lesion, this indicates that 78 per cent. of all restricted cases involve the cord or its nerve-roots to some extent. From the point of view of operability and functional result this is a matter of prime importance.

Complications.—In non-viable cases unassociated anomalies—hare-lip, ectopia vesicæ, non-paralytic club-foot and other more widespread abnormalities—are very common. In viable cases they are less frequent, but still sufficiently so to call for comment.

Nervous complications are of even greater frequency. Among 359 cases collected by the London Clinical Society, in which the complications are stated, 46 had hydrocephalus. These are cases in which the patients had restricted lesions. Harrar in the records of 68 cases in the Lying-in Hospital found 23 cases of primary hydrocephalus and 10 developing hydrocephalus following operation. The greater number which he found are doubtless due to the fact that his records include all cases observed, whether viable or not.

No facts regarding the incidence of hydromyelia are available. From my own very limited experience it appears to occur in a high percentage of those cases in which the cord is involved in the lesion, whether there be hydrocephalus or not. Thus in Cases I and VI there was hydrocephalus and hydromyelia above the open cord segments; in Cases III, IV and V there was hydromyelia without hydrocephalus. Information regarding the condition of the cord in the single case of meningocele reported (Case VII) is necessarily lacking. The small proportion of restricted cases which show sufficient dilatation of the cord to fall into the class of syringo- (or hydro-) myelo-meningocele, represents, therefore, only an exaggeration of a fairly frequent condition. Further investigation along this line is urgently needed. Post-mortem examination is not always essential to this, since careful examination of the cut end of the cord at the time of operation on cases with attached cord will reveal any considerable dilatation which may be present, and while the extent of this lesion upward may remain uncertain, it appears to be practically certain that a dilatation which is plainly visible at this point involves a considerable number of segments above. All cases in which complete autopsy findings can be obtained should be investigated with reference to this feature.

Paralyses of the sphincters or of the legs, and loss of sensation over areas supplied by nerves involved in the lesion, are encountered in the exact proportion in which one finds involvement of the cord in the lesion, and are a direct result rather than a complication of the disease.

Course of the disease.—A large proportion of untreated cases die within a few months. Thus of 649 deaths due to spina bifida, occurring in England in the year 1882, most of them in untreated patients, 612 were in the first year of life. Of 68 cases reviewed by Harrar (59 born in the Lying-in Hospital and 9 others sent in for operation) 7 were stillborn, and 29 died untreated within a few weeks. The other cases of his series were submitted to operation. Of 49 fatal cases of untreated restricted lesion collected by the writer, in which the cause of death is definitely stated, 14 died of marasmus, 7 of intercurrent infection, 2 of hydrocephalus, 23 of rupture of the sac, 3 of convulsious (i.e., meningitis). Accurate statistics of such untreated cases are very hard to obtain since untreated cases are but rarely recorded. In but a very small proportion even of the mild defects is there hope of recovery without operative interference, yet in a few of the less severe cases spontaneous cure occurs. In the 60 untreated cases recorded by the London Clinical Society, 14 cases (23·3 per cent.) were cured in the following manner: in eight there was a gradual shrinkage of the sac; in one it ulcerated and oozed for some time; in four it burst and later shrank away. The shrinkage of small tumours in this way probably accounts for a certain number of cases of spina bifida occulta, while others may be accounted for by a similar reduction of the tumour in intra-uterine life.

Operative mortality.—In Moore's series there was 27 per cent primary mortality, with an additional 7 per cent. within three months after operation, bringing the total to 34 per cent. When one considers that the cases which are operated upon are all selected cases, this primary mortality is exceedingly high; moreover, a secondary mortality is to be expected, apart from operative interference. Moore considers that "if all cases had been followed and reported, the probability is that the mortality at the time of, and a few months subsequent to, operation would be fully 50 per cent." In view of this he considers that operative interference in children under 5 years of age is scarcely worth while, since it appears neither to reduce the natural death-rate nor to be attended by great functional success. On the other hand he takes the position that children who have survived to that age may be submitted to the risk of operation.

As opposed to this view there is the great danger already alluded to, of rupture and ulceration of the sac. In 117 untreated cases collected from the appended bibliography, rupture of the sac occurred 27 times. In 97 of these cases in which the character of the sac is recorded, there was ulceration in 24. In the five restricted cases considered in this report, there was rupture in one, gross ulceration of the sac in two, and microscopical evidence of inflammation in the shape of polynuclear and round cell infiltration in four. One sac was not examined microscopically. In the case in which Morton's fluid was used death occurred immediately upon the injection, so that the inflammatory exudate was present prior to this treatment. Harmer found ulceration in 64·7 per cent. of his 34 cases. He further points out that he has found rupture of the sac in patients a few hours old, and suggests very early operation because of this danger and that of ulceration with subsequent meningitis. In view of the fact that few untreated cases are recorded it seems probable that these complications occur even more frequently than the figures would lead one to suspect. The primary operative mortality, so largely due to infection, might be materially decreased by very early operation, even though the secondary mortality, which depends mainly upon hydrocephalus and marasmus, be correspondingly increased. There appears to be no reason to consider that operation increases the percentage of hydrocephalus, in view of the large percentage occurring without interference and the number of cases that are accompanied by hydromyelia. It must be borne in mind in considering this that the majority of successfully operated cases (i.e., those which do not succumb to the immediate effects of operation, as shock, infection, &c.) live longer than do untreated cases, and therefore a higher percentage die of hydrocephalus which would otherwise have died of the meningocele itself (rupture, meningitis, &c.). Many surgeons, however, recognizing the high incidence of hydrocephalus, prefer to wait some months for its development before undertaking an operation which they feel may be useless.

Theoretical Considerations regarding Surgical Procedure.

Operability.—The question of operation upon cases with associated hydrocephalus, paralyses, &c., must remain largely a matter of individual opinion. It is purely from the point of view of the anatomical facts that I propose to discuss it. There can be no doubt that pure meningoceles should be operated upon, and in view of the possibility of ulceration or rupture of the sac they should be treated early. Moreover, shock is almost certainly less in operations upon the spinal cord of young infants than in older children. Spontaneous cure is not to be expected in the great majority of cases, and the risks run by awaiting it are too great. In the cases in which there is some doubt as to the presence of nerve elements in the sac, evidences of paralyses, especially of sphincters, and anæsthesia round the anal margin or on the back of the thighs, are of value. Ulceration of the sac wall, a thickened band down the middle of a thin sac wall, and a vascular granulating surface with umbilication, are valuable diagnostic indications of adherence of the cord. The presence of skin covering the whole of the sac does not rule out myelocele. It must be borne in mind that meningoceles are infrequent and myelomeningoceles frequent, but that but few meningoceles have broad bases. Transillumination of the sac has been suggested for finding the presence of nerve roots, but it seems possible that this might lead to error, as adventitious meningeal adhesions sometimes occur. In contemplating operation on those cases in which cord is known or suspected to be present, one should consider that in this type spontaneous cure is practically never attained ; that ulceration is exceedingly frequent and meningitis therefore the almost inevitable outcome ; that not only is the cord below its attachment to the sac practically useless, but the attachment is dragging upon the relatively normal cord above and jeopardizing its function. This is a matter which has not been given due weight in considering the advisability of operating in this type of case, though the traction on the cord has been recognized by all careful investigators, as is shown in the diagrams of my cases. Damage already done cannot be repaired by relief of tension, but at least the conditions can be rendered more nearly normal for the further development which goes on after birth.

Methods of treating the sac.—Stress has always been laid upon the careful dissection of nerve roots from the sac wall, and rightly so, if they be attached to a relatively normal cord. Many observers, however, have recognized that the nerves were inseparably bound to the wall of the sac and have failed to realize the true significance of this. They have not seen in the thickened band of sac roof, to which nerve roots pass, the malformed, practically useless segments of the cord without which the nerve radicles are valueless, and have dissected free roots that could serve no purpose. La Ferte and others, recognizing the importance of preserving the cord, have attempted to turn in the portion of sac wall to which it is attached, with the result that meningitis has followed with great frequency. When one considers that it is almost impossible to dissect free any of this attached part of cord, and that inevitably one must leave some skin with it if one preserves all the nervous elements, the avoidance of meningitis becomes practically impossible. Nor does it appear to be wise to make this attempt in view of other matters. The cord segments distal to the point of attachment to the sac roof, as shown in this report and in other similar cases reported by previous investigators, are so poorly developed and so damaged by inflammation and epidermal overgrowth, that they are practically functionless; this can be demonstrated histologically and by the neurological examination of the regions normally supplied by them. There is, therefore, nothing to be gained by their preservation. All that can be hoped for is that the segments above the cord lesion may be so far as possible preserved from further harm. To accomplish this the end of the cord must be cut free and allowed to slip up into the canal.

An adherent plug of sac wall left by the operator is comparable anatomically to the adhesion of skin or fibrous tissue to the cord found in spina bifida occulta. Theoretically at least delayed traction or pressure symptoms may be expected here as in the primarily occult cases. Nor can one overlook the danger of an inclusion dermoid developing from the buried epithelial cells of the sac wall. This is especially the case where skin covers or almost covers the whole of the roof of the sac, for in such cases deep skin glands may lie in almost direct contact with the lateral parts of the cord tissue. These delayed effects are not ordinarily reported, because but few cases where the patient survives to adolescence report to the surgeon who has operated, and this is probably particularly true of the cases with new symptoms. Such patients, dissatisfied with the result of the first treatment, are likely to seek some other surgeon who is ignorant of the precise anatomical state and method of procedure at the primary operation. It is difficult to trace successful cases after a number of years have elapsed; it is even more difficult to trace failures. In the light of the anatomical condition in cases with attached cord, therefore, the rational procedure is to cut free the cord as close to sac wall as is possible without leaving any attached inflammatory or surface epithelium, and to injure as little as possible by ligature or by handling the end of this normal cord and the nerve roots attached to it. From purely theoretical reasons it would appear to be preferable to ligate the anterior median vessels with very fine ligatures without including the entire cord, since compression of the cord within the pia must pulp a considerable portion of it. Exceedingly delicate ligatures and a very fine needle should be used for this, and the ligatures used as tractors to steady the cord while it was being freed from the sac wall. With a view to preserving as much as possible of the healthy cord the line of section should be made parallel with the sac roof and not transversely across the cord.

Attention must also be directed to the nerve radicles which arise from the intra-cystic portion of the cord. Nerve roots in connection with the stretched segments within the sac run in contact with the cord until they reach the roof of the sac. To this they are adherent, and from this course back freely through the sac to their foramina. This fact is demonstrated in Cases III, IV and V. The difficulty in recognizing them is caused by their abnormal direction and adherence to the sac, so that they appear to arise from the involved segments of the cord in the sac wall. If the intra-cystic portion of the cord is carefully examined these roots may be traced from their origin and should then be carefully freed from the sac wall before the cord is cut free. If the anatomical relations are kept clearly in mind the recognition and dissection of these roots should not be impossible under the conditions of operation. The increase in paralysis after operation, often encountered in this type of case, is probably in many instances due to section of these radicles, and not to the section of radicles which arise from the segments of cord which are adherent to the sac wall.

Post-operative recovery.—Except in the cases of spina bifida occulta with pressure symptoms, and in a small number of meningoceles in which there is adherence or traction of the nerve roots but no lesion of the cord, no improvement in function is to be expected as the result of operation. What may be hoped for is that the function of segments above the lesion will not be subjected to further impairment by the traction of fluid or the presence of inflammation. In but few cases even of pure meningocele is there perfect function of the sphincters. This leads one to suspect some cord involvement, perhaps only to the extent that the closed cord is drawn down out of its normal level into the floor of the sac. This probably indicates, as noted in the description of Case VII, that the initial lesion was in the neural ectoderm and that the development of the lower segments of the cord was interfered with to some extent. In operating upon these cases, therefore, one must be prepared for some loss of function of the sphincters, and must remember the great difficulty of determining this accurately in the very young infant. It appears to be practically impossible in many cases to determine without undue risk to the patient whether the nervous tissue lying in the floor of the sac is the cauda equina, as it should be in a lumbo-sacral tumour, or the end of the cord itself. Nevertheless, this should be determined as nearly as possible, and where there is any doubt in the matter this doubt should be stated definitely in the notes. After reading many case reports in which cord and nerve radicles were said to be absent from the sac, and yet there was incontinence of urine and fæces either before or after operation, one cannot help feeling that some uncertainty existed at the time the observations were made. This is a matter of considerable importance for the surgeon, since the operation which is followed by incontinence where none has been predicted is distressing, and leads the parents to blame the operator though he may not be at fault.

Where there is paralysis of the legs, it may be taken to indicate almost certainly that there is an adherent cord in the sac, and in view of its poorly developed and degenerated condition it may be further assumed that the paralysis is not remediable, even in the rare cases in which circumstances will permit the preservation of part of the degenerated cord. For the purpose of prognosis and also for the advancement of the general scientific knowledge of the subject, the sac wall in such cases should be submitted to systematic microscopic examination. Until this is done and careful reports of the state given with case reports, the results of different methods of treating the sac, and especially the prognosis of different types of case as regards late functional results, cannot be raised above the level of speculation. In this connection it may not be out of place to recall the statistics of Saachtleben (quoted from Harrar), who found in an analysis of thirty cases from the Mikulicz clinic that five only were permanently cured, and these were meningoceles. Harmer in his thirty cases found some paralysis in twenty. This was increased after operation in three; not affected in nine; and improved in eight. Of these eight, five were slightly improved but died subsequently of hydrocephalus or infection. One with pre-operative incontinence showed improvement fifteen months later; one with paralysis of the foot and loss of sensation in both legs recovered from the paralysis but showed no change in the sensory loss; one with paralysis of the legs was well sixteen months later. From this evidence, Harmer concludes that paralysis is in some cases due to traction: a strong argument in favour of operation on cases with attached cord.

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OBSERVATIONS ON CEREBELLAR STIMULATIONS.

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THE question whether the cerebellar cortex is capable of responding to electrical and other forms of stimulation is at present unsettled.

André-Thomas [1], who gives a résumé of the earlier literature, notes that stimulations evoke less constant effects than experimental destructions. He also comments on the great diversity of opinion expressed: some observers attribute definite responses to the various regions stimulated; others deny the excitability of the cortex, whilst admitting it for the intracerebellar nuclei.

The view last expressed is that maintained by Horsley and Clarke [7], who ascribe the results occasionally yielded by cortical stimulation to spread of current to the intracerebellar nuclei. They emphasize a fallacy, which doubtless entered into much earlier work, namely, the facility with which the effects of excitation may be vitiated by current escape to the nucleus and rootlets of the accessorius nerve.

As the outcome of researches on the dog and monkey, Rothmann [9] arrived at conclusions which diverge materially from those of Horsley and Clarke. Stimulating with the bipolar method, the animal being in morphine-ether narcosis, he found the threshold much higher than that of the cerebral cortex. Whilst admitting that some movements of the fore-limb may be due to current diffusion to the intracerebellar nuclei (dentate nucleus), he considers that certain characteristic toe movements in the fore-leg, elicitable from the anterior surface of the cerebellum, are an expression of genuine cortical excitation. He was able to prove that the impulses concerned in this response are conveyed by the superior peduncles and rubrospinal tracts.

It should be remarked in passing that the conclusions of this writer show but little agreement with the localization theory of Van Rynberk [10]; this theory has more recently been accorded the support of André-Thomas and Durupt [2].

Although Rothmann fails to comment on the mode of causation of the "running movements" ("Laufbewegungen") at times elicitable from the anterior part of the vermis, it is probable that he considers them due to excitation of the cortex. It may be inferred, then, that he regards the cerebellar cortex as excitable.

Beck and Bikeles [3], who repeated earlier experiments of Magnini, conclude that strychnine and phenol are without action on the cortex cerebelli, and, therefore, assert that it is inexcitable.

Shimazono [13], however, applied strychnine to the cerebellar cortex of the pigeon and observed an increase of muscle tonus on the same side of the body.

Beck and Bikeles [4], reverting to the problem, deny any increase of tonus in either pigeon or dog as a result of the action of strychnine on the cortex and, in consequence, reaffirm their original thesis that the cortex is inexcitable.

After denying the excitability of the cortex, the same authors assert, with curious inconsistency, in a subsequent paper [5], that cooling does not depress the *excitability* of the cortex. Failure to mention any definite reactions makes it appear probable that, whatever responses may have been induced, they were excited by action of the current elsewhere than on the cortex (trigeminus, accessorius or nucleus gracilis or cuneatus, *vide* Horsley and Clarke [7]). Such an interpretation would afford a plausible explanation of the lack of change on cooling.

Similar criticisms apply to the conclusions of Bikeles and Zbyszewski [6] that cocaine does not lower the excitability of the cortex.

Consideration of the conflicting statements outlined above reveals the desirability of further evidence regarding the question of the excitability of the cortex cerebelli. The idea that the cortical neurones are excitable appears natural and logical, and its proof demands only the selection of a suitable test reaction, which might be evoked by currents of low intensity, the action of which would extend but a slight distance below the surface.

A reaction fulfilling these conditions was described by Sherrington [11]: when the anterior surface of the cerebellum is faradized there ensues an immediate inhibition of the "decerebrate rigidity" previously evoked by ablation of the cerebral hemispheres. Accordingly, this inhibitory response was employed in the present research as a means of deciding the question whether the cerebellar cortex is excitable.

In the course of this work faradization was applied to the superior cerebellar peduncle in a few instances. The only previous observations on this subject which have come to our notice are those of Thiele [14]. As a result of such stimulation he observed, in particular, movements of the ipsilateral fore-limb consisting of protrusion at the shoulder and flexion at the elbow.

METHODS.

The bipolar method of stimulation was chosen in the majority of experiments, since it appeared that the current would be confined to the cortical layers of neurones in a manner scarcely possible in the unipolar method. The platinum electrodes terminated in small beads 1 mm. apart. When precise localization was necessary recourse was had to the unipolar method, the stigmatic electrode being of the usual Sherrington type. The inductorium was operated by two storage batteries; an ammeter and rheostat were included in the primary circuit and the resistance was so arranged that, whilst the hammer was in vibration, the ammeter showed a reading of approximately 0·2 ampère. At 135 mm. secondary distance the current from the bipolar electrodes was just detectable on the tip of the tongue.

The animal (cat) was anæsthetized with chloroform and ether. Tracheotomy was performed and both carotids were ligated. Decerebration was performed with the decerebrator [12], the plane of the section lying about 27 mm. behind the frontoparietal suture, in a cat of medium size. The level of this section, somewhat anterior to that usually employed, was chosen on account of the necessity of preserving the tentorium cerebelli intact. The plane lies usually just in front of the posterior colliculi. Following the decerebration a small serrefine was clamped on the divided basilar artery. The latter procedure permitted of the immediate continuance of the experiment. The head was then supported at a convenient height in a clamp applied either to the lower jaw or to the skull. Precautions were observed to keep the cortex in normal condition by the application of swabs wet with warm saline solution.

RESULTS OBTAINED IN PRESENT INVESTIGATION.

When stimulation of appropriate strength is applied to the anterior surface of the vermis[1] there results an immediate and general relaxation of the rigidity. The possibility that this inhibition is evoked, to any important degree, from the cut edges of the dura or through the trigeminus may be quickly excluded. The low intensity of the current (100 mm. sec.) and the position of the electrodes in the mid-line render it practically certain that no physical spread can occur to the dural margin or to the trigeminus, both of which are too far distant. Furthermore, we found that the application of 1 per cent. cocaine hydrochloride to the edge of the dura did not modify the reaction in any way. Hence, it may be concluded that the inhibition is evoked from the cerebellar substance.

Possible influence of the current on the internal nuclei in contributing to the effect must next be considered, and the evidence which renders this factor unessential will now receive attention.

In the first place a "healthy" vascular condition of the cortex is necessary for the production of the response by weak currents. The development of anæmia immediately abolishes the reaction. In these respects the cerebellar cortex closely resembles the cerebral cortex. Moreover, the inhibition is elicitable by weak currents (100 mm. sec.), which are, indeed, less intense than those required to excite the cerebral cortex; in one experiment the threshold for exciting hind limb movements from the cerebral motor area was not attained until the secondary coil was at 58 mm. This observation is contrary to those of Beck and Bikeles [5]; the possibility, however, has already been suggested that some, at least, of the reactions described by these writers were caused by current escape to the trigeminus or accessorius, rather than by direct stimulation of the cerebellar cortex. Under these circumstances the current strengths they employed would not indicate the degree of excitability of the cerebellar cortex. In support of such an interpretation of their results, we would mention that we observed that approximation of the electrodes to the vicinity of the trigeminus yields marked postural changes in the ipsilateral fore-leg, and that direct stimulation of the nerve itself with weak currents (200 mm. sec.) causes flexions and claw movements in the same limb.

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[1] The terms "vermis" and "lateral hemispheres" are retained in the present paper, since the nomenclature of Bolk and van Rynberk offers no advantages in relation to the problems investigated.

If we admit that the inhibition is called forth in the cortical neurones we may naturally expect abolition of the response by the application of cocaine. Accordingly, the response was induced from the anterior surface of the vermis by a minimal current and a 1 per cent. solution of cocaine hydrochloride containing a little methylene blue was then applied. Stimulation of the original intensity repeated after about one minute yielded no response. It is reasonable to suppose that the influence of the cocaine was mainly on the cortical neurones and that, therefore, the inhibition had been induced as a result of excitation of these neurones.

The evidence given above leads to the logical conclusion that the inhibition is induced as a consequence of a state of excitation in the cortical neurones or, in other words, that in respect to this reaction the cerebellar cortex is excitable.

Sherrington [11] describes the "inhibitory area" as extending over the anterior surfaces of the vermis and lateral hemispheres. With the intention of studying the cortical distribution of the response, we explored the cerebellar surface in other situations. In one experiment small portions of the vermis were successively exposed and each portion was tested with a weak current (98 mm. sec.). It was found that the vermis yielded inhibition from its most anterior part backwards to about 3 mm. above the medulla oblongata; farther than this it was impractical to go, owing to action of the current on the medullary centres. The inhibition affected all four legs; although the remainder of the body was not observed specially, it probably shared in the reaction.

Conclusions regarding the results of faradizing the anterior surface of the lateral hemisphere are only permissible when currents of low intensity are employed. In the case of stronger currents the possibility of diffusion to the cut dural margin or to the trigeminus or accessorius must be considered. Sherrington observed modifications of the rigidity as a result of stimulation of the edge of the dura. He also noted alterations induced reflexly through the trigeminus [11], whilst we ourselves (*vide supra*) obtained changes in limb posture as a result of the action of weak currents on this nerve. Our observations showed that the inhibition elicitable from the anterior surface of the lateral hemisphere reveals itself most intensely in the ipsilateral limbs and more noticeably in the hind-leg than in the fore-leg. Fig. 1 indicates the extent of the anterior cerebellar surface, on one side, from which the reaction was evoked.

The effects elicitable from the posterior surface of the lateral hemisphere have not yet been studied sufficiently to permit of drawing definite conclusions.

In a number of experiments faradization was applied to the superior cerebellar peduncle. In one experiment the cerebellum was removed; subsequently the rigidity first increased and then disappeared completely (cf. Weed [15]). Bipolar stimulation of the right superior peduncle (82 mm. sec.) then yielded rhythmical opening and closing of the claws of the right fore-leg together with running movements in both hind-legs. The unipolar method was then substituted, the indifferent electrode being secured to the left hind-leg. Stimulation was applied to the same situation as in the bipolar method, the secondary being at 100 mm. There resulted the same type of claw movements in the right fore-leg; these movements are very characteristic and resemble those noted in a stroked cat. Because of the attachment of the indifferent electrode the hind-legs were not observed.

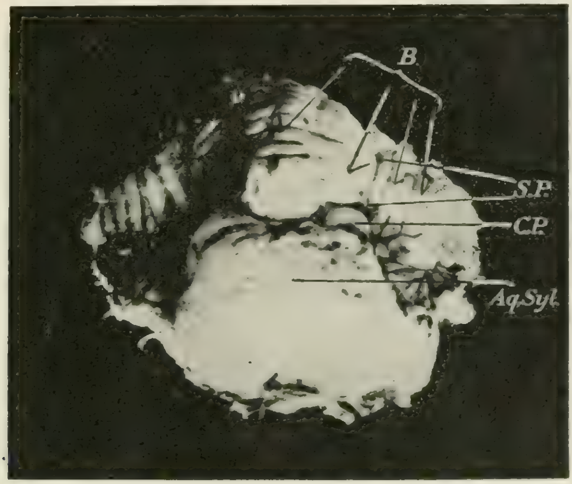

FIG. 1.—Anterior surface of cerebellum of cat. × 2. Aq. Syl., aqueduct of Sylvius B, bristles indicating extent of "inhibitory area" on one side; C.P., colliculus posterior; S.P., sulcus primarius (Bolk).

A bristle was inserted at the point yielding the reaction just depicted. Sections were prepared and were stained by the Weigert hæmatoxylin method. The bristle is found, on examination, to be situated in the right brachium conjunctivum (fig. 2). The electrode was applied at the point of entrance of the bristle into the brain-stem.

That the effects just mentioned are in reality due to stimulation of the brachium conjunctivum and are not caused reflexly is rendered practically certain, since claw movements of the same character were elicited by faradization of a point in the interior of the cerebellum at a particular stage in its removal. In this instance a tract destined to enter the brachium conjunctivum was doubtless stimulated.

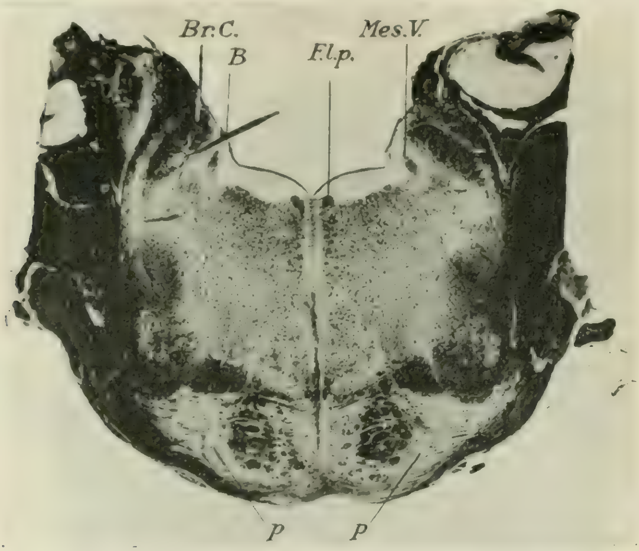

FIG. 2.—Section through the pons of a cat's brain. × 6. *B*, point of entrance of bristle, indicating position of electrode by which claw movements were evoked in right foreleg; *Br.C.*, brachium conjunctivum; *F.l p.*, fasciculus longitudinalis posterior; *Mes.V.*, mesencephalic root of trigeminus; *P.*, pons.

We may conclude, therefore, that stimulation of the brachium conjunctivum induces claw movements in the ipsilateral fore-leg. With respect to the exact localization of the running movements of the hind-legs evoked by bipolar stimulation, further experiments are in progress.

Thiele [14], whose observations on stimulation of the superior peduncle were cited in the introduction, does not mention the occurrence of reactions like those noted in our experiments.

A variation from the usual inhibitory response of the cerebellum was noted in a few instances. Stimulation of the anterior surface of the vermis over the area outlined in fig. 3 resulted in the following sequence of events.

(1) Inhibition of rigidity in both fore-legs;

(2) Increased rigidity in the right fore-leg and inhibition of rigidity in the left fore-leg;

(3) Walking movements of the fore-legs, during which the increase and decrease of tonus appeared reciprocally in the two legs.

Concurrently with these fore-leg reactions there developed in the hind-legs first walking and later running movements; movements of the claws also occurred in the hind-legs. The running movements recall the "Laufbewegungen" of Rothmann [9].

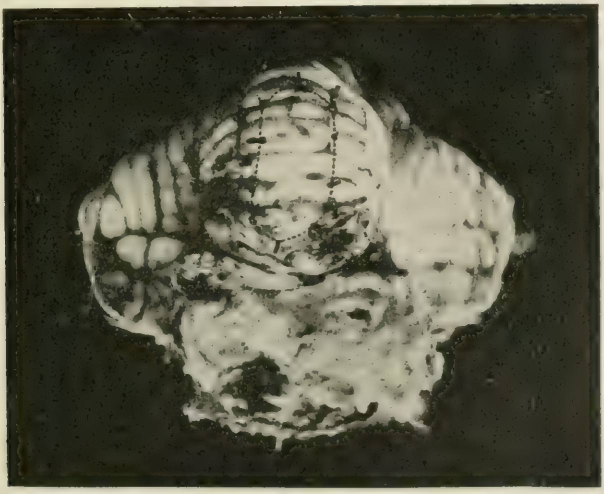

FIG. 3.—Anterior surface of cerebellum of cat. × 2. Faradization of area enclosed by dotted lines yielded walking in fore-legs and walking and running in hind-legs. The figure shows the specimen after removal of part of the mid-brain subsequent to evoking the reactions described.

During the course of another experiment, in which stimulation of the same region yielded mainly inhibition of all fore-legs, it was once noted that a few walking movements of the hind legs resulted.

Since the walking and running movements just mentioned may be evoked with currents of low intensity which at times yield inhibition, and since the inhibition itself has been shown to be a cortical response, it is logical to conclude that the walking and running movements are also an indication of cortical activity. Hence these observations afford additional evidence in favour of our main thesis that the cerebellar cortex is excitable.

SUMMARY.

(1) Evidence is adduced to prove that the cerebellar cortex is excitable. The reaction chosen as a test was the inhibition of decerebrate rigidity evokable by stimulation of the surface of the cerebellum. Reasons are given for concluding that this reaction is induced as the result of a state of excitation in the cortical neurones of the cerebellum.

(2) The inhibition is yielded by the greater part of the vermis in an antero-posterior direction; it is also yielded by the anterior surfaces of the vermis and lateral hemispheres.

(3) Stimulation of the brachium conjunctivum causes claw movements in the ipsilateral fore-leg.

(4) Excitation of the anterior surface of the vermis occasionally elicits, as an alternative to inhibition, walking movements of the fore-legs and walking or running movements of the hind-legs. Since these reactions, like the inhibition, are induced by weak currents, they support our contention that the cerebellar cortex is excitable.

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THREE CASES OF SUPRA-PITUITARY TUMOUR PRESENTING FRÖHLICH'S SYNDROME.

BY CHARLES N. ARMSTRONG, M.B., D.P.H.DURH.

THE three cases about to be described are instances in which Fröhlich's syndrome was present in a more or less pronounced form associated with unusual types of tumour in the base of the brain, none of which started in or infiltrated the pituitary body. In the first two cases the tumour was a cystic ependymoma, and in the third case a cholesterin-containing cyst.

Case 1.—E. H., male, 10 years of age, was admitted to the National Hospital, Queen Square, under Dr. Gordon Holmes, on October 10, 1921, complaining of failing sight, headache and vomiting. His mother stated that the headaches and stiffness of the back of his neck began four months previously: the headaches occurred each afternoon, usually when he was returning home from school. Some weeks later he became subject to vomiting. After the summer holidays he returned to school on September 19, but remained there only a week; it was reported that he was not so bright as formerly and suffered from "heat-waves."

About September 29, after a restless night he complained of severe headaches; his pupils were dilated, he vomited about 10.30 p.m., and again a little later, and became drowsy.

His sight had been deteriorating since August and sometimes he complained of seeing double on looking straightforward. Three weeks before admission to hospital his mother noticed that his left eye squinted, turning inwards. This condition recurred once. During the last few months he had become much fatter.

No previous symptoms had been noticed, except that for the preceding two to three years he had complained of his hands being cold.

Examination.—A finely-featured well-nourished small boy 10 years of age, but he looked younger than his years. Height 3 ft. 10 in.; weight 3 st. He was very drowsy and spoke in a somewhat tired manner with a hoarse voice. His skin was dry and exceptionally smooth and delicate. He was rather adipose generally with a feminine type of fat distribution over hips, abdomen, pubes and chest. The hands were small with long tapering fingers; his feet also were small and finely formed. The external genitalia seemed normal.

No loss of sense of smell was detected. Visual acuity was much reduced on admission: he could only see the largest letter on Snellen's Chart at bed length ($\frac{2}{60}$), vision being somewhat better in the right eye than in the left.

There was advanced papillœdema in both eyes, the swelling in the right reaching 3 D., and in the left 2 D.

The discs were becoming white and opaque-looking, and their vessels diminished in calibre.

Examination of the fields of vision was very difficult, as patient was very drowsy and difficult to arouse: they seemed reduced in the temporal halves and also to some extent in the nasal halves. The movements of his eyes were full. His pupils were dilated, circular and equal, reacting feebly to direct light and on accommodation. No abnormalities were detected in the function of the other cranial nerves, and the motor and sensory systems and the reflexes were unaffected.

His heart, lungs and alimentary system were normal. The systolic blood-pressure was 106 mm. Hg. Radiographic examination showed that the sella turcica was enlarged, chiefly in the antero-posterior plane. Unfortunately examination of the sugar tolerance could not be made as the administration of glucose caused vomiting.

On October 18, a right-sided parietal decompression operation was performed by Mr. Percy Sargent. About fourteen days later the patient was much improved; he was not so drowsy, had no pain and was brighter. His visual acuity increased to $\frac{2}{24}$.

As the ultimate prognosis seemed hopeless a second operation was undertaken for the removal of the tumour on November 2. The tumour was reached from the fronto-orbital route, the capsule opened and part of it removed by suction.

Post-operative notes.—The patient took small feeds quite well in the afternoon and the evening of the day of operation but did not regain full consciousness. The pulse was rapid and often difficult to feel. He collapsed and died in the early morning of the following day.

Pathological investigation.—A post-mortem examination was made on the same day. On removal of the brain a large tumour was found above the optic chiasma which it displaced downwards. After making a sagittal section through the brain, the tumour was seen to be in the mid-line; it was about the size of a walnut and was attached to the floor of the third ventricle throughout its whole length, and also to the infundibulum from the upper part of which it appeared to arise. The tumour was surrounded by a capsule except where it was united to the upper part of the infundibulum. It was semi-cystic and contained a highly-albuminous yellowish serum with numerous cholesterin crystals and some calcareous matter (fig. 1).

The sella turcica was greatly enlarged, evidently as a result of the absorption of bone, while the posterior wall of the fossa had been pushed backwards by the tumour. The pituitary body itself appeared to be of normal size though flattened by pressure.

A section through the infundibulum and that part of the tumour adjacent

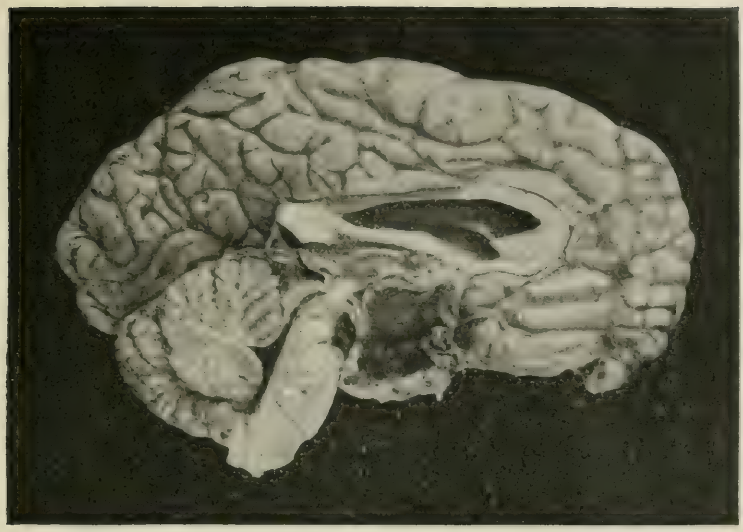

FIG. 1.—*Case* 1. Mesial sagittal section through brain, showing left half of tumour in position.

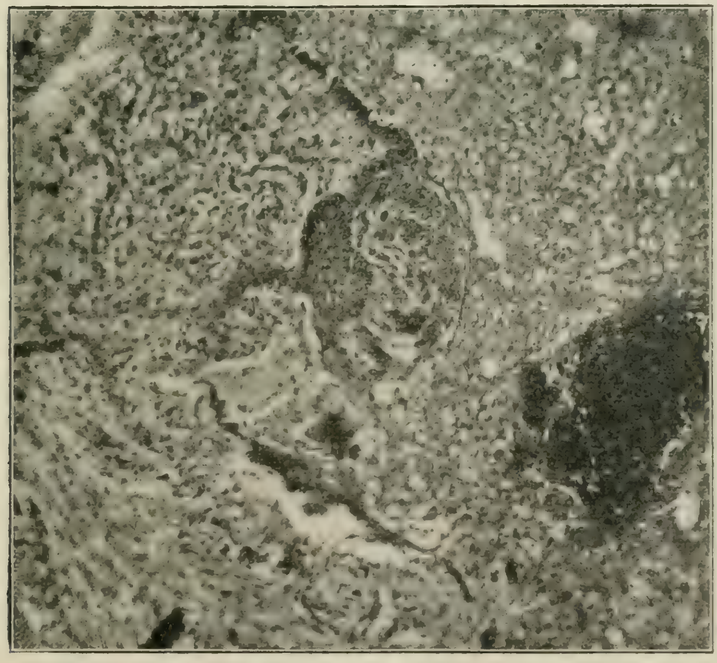

FIG. 2.—*Case* 1. Photomicrograph of section through the infundibulum and that part of the tumour adjacent to it, showing the proliferation of the cells of the ependymal lining of the recessus infundibuli. On the right side of the ependyma the normal neuroglial tissue of the infundibulum can be seen and on the other the cavity of the tumour containing organizing serum and calcareous deposits.

to it shows that the tumour is intimately connected with, and probably originated from, the ependyma of the infundibular recess (fig. 2). On the one side of the ependyma is the normal neuroglial tissue and on the other part of the cavity of the tumour containing organizing serum, some polymorphonuclear and mononuclear cells with pyknotic nuclei, and small areas of calcareous deposit. In the portion shown in fig. 2 the ependymal cells have proliferated and penetrated in both directions, but to a less extent into the glial tissue than into the tumour mass. Isolated clumps of these cells could be seen scattered through the infundibular tissue, while the tumour itself appears to be composed of strands of such cells enclosing spaces filled with serum and fibrin in which there are numerous calcareous deposits. These strands of epithelial tissue run in a matrix which is indistinguishable from glial tissue, and in this tissue run the blood-vessels which are numerous and have thin walls. The outer cells of these epithelial masses are columnar and the others polygonal. The central parts of the epithelial masses tend to degenerate and to be replaced by fibrin or calcareous tissue. The appearance suggests that many of the spaces are formed in this way by disintegration of the tumour.

Case 2.—F. S., aged 35, female, was admitted to the National Hospital, under Dr. Gordon Holmes, on November 29, 1919, complaining of blindness, headache and adiposity. She gave the following history of her illness. Fifteen months previously amenorrhœa commenced; then she began to get fatter, felt tired, and about the same time noticed a slight alteration in her sight. Vision became worse nine months later and occasionally she had diplopia. During the last two weeks vision had deteriorated very much and light irritated her eyes so that she wanted to keep them closed. She had suffered from slight headaches for a long time, especially in the mornings, but they had become much worse during the past month and had been accompanied by vomiting for the last week. She thought that she passed more urine than formerly.

At the beginning of her illness she weighed 11 stone.

Examination.—An enormously fat, but otherwise healthy looking woman; weight 16 st. 6 lb. Her skin was fairly fine, but very dry and soft. There was no alteration in the body hair except perhaps that it was somewhat sparse, but the hair of her head was thick and normal in appearance and quality.

No loss of sense of smell detected Visual acuity of the left eye was $\frac{6}{60}$ and that of the right even less.

Perimetric examination revealed a partial scotoma for white in right inferior quadrant of right eye, and indistinctness of vision in the rest of the temporal field. No scotoma for white was detected in the left eye.

She was unable to recognize red or green in the region of the fixation point in either eye, but her headaches were so severe that complete examination was not possible. Her optic discs appeared normal. Her right pupil was slightly larger than left; both were circular, and reacted to direct and consensual illumination. There was complete paralysis of right external rectus, the other ocular muscles being normal, but the left eye developed nystagmoid jerks on looking to the right. No abnormalities were detected in the functions of the other cranial nerves, and the motor and sensory systems and the reflexes were normal.

Her systolic blood-pressure was 121 mm. Hg, the diastolic being 82 mm. Hg.

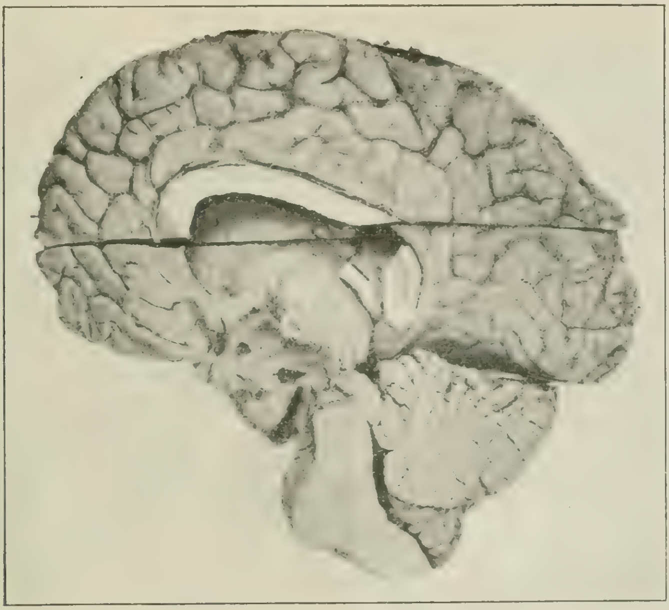

FIG. 3.—*Case* 2. Mesial sagittal section through brain showing right half of tumour in position.

Radiographic examination showed no evidence of enlargement of the sella turcica in the antero-posterior plane, but viewed stereoscopically it appeared enlarged laterally. The sugar tolerance was not above normal, 100 grm. of glucose giving rise to glycosuria.

On January 24, 1920, a right temporo-parietal decompression operation was performed by Mr. Percy Sargent; there were evidences of an enormous increase of intracranial pressure. Patient died five days later.

Pathological investigation.—A post-mortem examination was made on the day after death. On removal of the brain a tumour about the size of a walnut was found in and above the sella turcica. It lay slightly to the left of the mid-line, behind the chiasma which it had pressed forward. In a sagittal section through the brain the tumour was seen to be semi-cystic, and to be attached to the floor of the third ventricle throughout its whole length (fig. 3).

There was very great enlargement of the pituitary fossa, chiefly at the expense of its anterior margin. The posterior clinoid processes were also pushed backwards.

On microscopical examination the tumour tissue is seen to be composed of branching epithelial masses of various shapes projecting in all directions and enclosing cystic spaces (fig. 4). Some of these cystic spaces contain a serous looking substance, and others organizing fibrinous matter. Calcareous deposits are also found within them. The cells of the outer layer of the epithelial masses which are in contact with these spaces are columnar and the more centrally placed are polygonal. Occasionally in the central area of some of the strands the cells are flattened. In that portion of the tumour adjacent to the brain there is a large amount of glial tissue intervening between the branching cellular processes. The blood-vessels are scanty and thin walled; they lie within the spaces and tend to channel the epithelial strands.

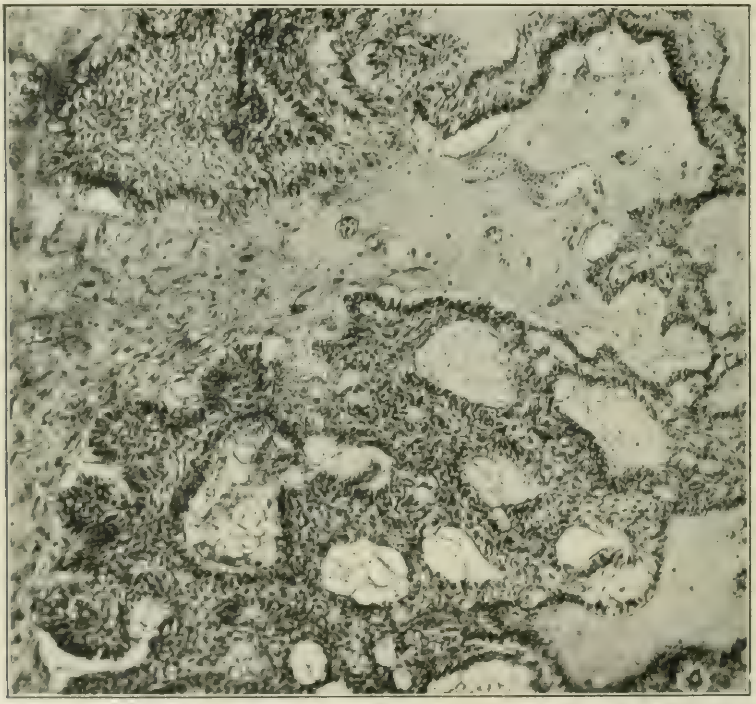

FIG. 4.—*Case* 2. Photomicrograph of section of that part of the tumour adjacent to the infundibulum showing branching epithelial masses enclosing cystic spaces and neuroglial tissue intervening between the epithelial processes.

Case 3.—W. L., aged 18, female, was admitted to the National Hospital under Dr. Farquhar Buzzard, on February 12, 1920, complaining of headache and loss of sight. Although 18 years of age she had never menstruated. Two years before admission she had begun to complain of frontal headaches which were worse each morning. She did not suffer from vomiting until twelve months before admission when it commenced accompanying the headaches and having no relation to food. About two months after the headaches began her vision became blurred, so that she could neither see to read nor to thread a needle. Her mother stated that at first she used to bump into people who were walking at her side as she could see only in front of her, and that she had to turn her head to look to either side. She had always been fat; before Christmas, 1919, her face assumed a bloated appearance, but this had become less pronounced. She was rather drowsy and was always dropping off to sleep.

Examination.—The patient was a very fat girl of 18 years who appeared to be only 12 to 14 years of age; she had a childish voice, and was of cheerful disposition. Her skin was abnormally dry and scaly. There was very little body hair, only two to three hairs in the axillæ and very few over the pubis, but the hair of her head was fairly long, thick and silky.

No loss of sense of smell was detected. Visual acuity was so diminished that she could only appreciate coarse hand movements. It was impossible to test her visual fields owing to failure of sight. Ophthalmoscopic examination revealed primary optic atrophy in both eyes. Her pupils were widely dilated, the left being slightly larger than the right. No reaction to light nor to accommodation was obtained in either. Both external and both internal recti were weak,and there was a divergent squint which became a little less marked when she tried to converge. No abnormalities were detected in the functions of the other cranial nerves, and the motor and sensory systems and the reflexes were normal.

The heart, lungs and alimentary system presented no marked abnormalities. The systolic blood-pressure was 100 mm. Hg, the diastolic being 70 mm. Hg. Sugar tolerance: 100 grm. of glucose given orally did not produce glycosuria. Other tests with larger quantities of glucose failed, as the patient vomited. Radiographic examination showed that the sella turcica was much larger than normal.

An operation was undertaken on March 20, by Mr. Percy Sargent. After a frontal osteoplastic flap, hinged in the temporal fossa, was made the frontal lobe was elevated and the tumour reached. A large quantity of yellow fluid containing numerous shimmering cholesterin crystals was removed from it by aspiration. After the operation the patient became almost maniacal, talking incessantly, was very restless and tried to get out of bed. A few days later her temperature began to rise and reached 106° F. An urticarial rash appeared on the back and buttocks. A lumbar puncture was performed and no evidence of meningitis was found. She died on April 2.

Pathological investigation.—A post-mortem examination was made on the following day. On lifting the frontal lobes of the brain, a tumour about the size of a walnut was seen filling the sella turcica with the optic nerves stretched over it. The sella turcica was appreciably enlarged laterally and antero-posteriorly but was not abnormally deep. An attempt was made to dissect the tumour from the surrounding tissues but in doing so the cyst burst and much brownish fluid with numerous plate-like crystals of cholesterin escaped. A few large solid masses of crystals were also found within it, and one plate of hard calcareous matter was seen attached to the upper wall of the cyst. In a sagittal section through the brain the tumour was seen to lie in the mid-line. The wall of the cyst was firmly attached to the floor of the third ventricle and to the infundibulum from which it apparently had arisen (fig. 5).

A portion of the cyst wall examined microscopically was seen to be formed of fibrous tissue only; no epithelial cell masses could be detected in it.

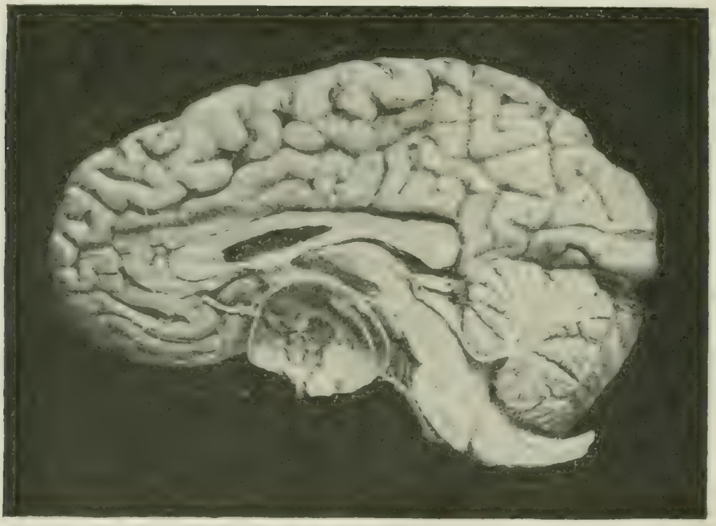

FIG. 5.—*Case* 3. Mesial sagittal section through brain showing right half of cyst in position.

In the first two cases described above the semi-cystic tumours were apparently of the same nature. The tumour tissue was composed of nests and branching masses of epithelial cells, enclosing cystic spaces, the serous content of which was in the process of organization. These epithelial masses were made up of several layers of cells; the basal cell layer being composed of columnar cells while the cells of the superimposed layers were chiefly polygonal. This epithelial tissue appeared to originate by the proliferation of the ependyma lining the recessus infundibuli. In fact this was fairly definitely shown in the first case. The calcareous deposits seen within the cystic spaces seemed to have been formed as a result of degenerative changes having taken place in the organized tissue within the spaces.

This type of tumour cannot be regarded as being entirely encapsuled, for in Case 1 there was evidence of its extension into the brain tissue near its place of origin.

Similar solid or semi-solid epithelial cell tumours occurring in relation to the infundibulum and third ventricle have frequently been described. The tissue from which this type of tumour originates has always been a matter of some speculation. Mott and Barratt [15] describe two cases, one of which they assumed originated from the choroid plexus, or from the lining epithelium of the infundibulum or of the third ventricle which it filled. Another, which resembled a papilloma, they regarded as an epidermoid cyst developed from misplaced ectodermal cells intended to form the scalp. Here the epithelial structure of the neoplasm bore a very close resemblance to the rete Malpighii of the skin, although no hairs nor fatty matter were present. Langer [10] also described two cases of papillary cysts which he regarded as definitely of infundibular origin.

Hecht [7], in 1909, described a tumour which very closely resembled the tumours in Cases 1 and 2, except that it contained some typical osteoid tissue which, however, may have been a fragment of the sella turcica, since the bone here was markedly corroded and thinned out. In a case described by Otto Kankeleit [9], a remnant of the eroded wall of the sella turcica was found in the tumour. The parenchyma of the tumour described by Hecht was considered to have been formed by proliferating cells of the pars anterior of the pituitary body. The cells formed alveoli-like spaces in a stroma of very loose vascular embryonal connective tissue composed of stellate cells. These alveoli were either completely filled with epithelial cells, or there was present only an outer shell of epithelial cells and an inner mass of hyaline material. The tissue in the interior of the spaces looked somewhat like "epithelial pearls" of cornifying carcinomata, although the material did not show any true cornification. The epithelial cells forming the follicular spaces were cuboidal or short columnar cells. These cells had not only formed the alveolar spaces but had also proliferated in a very irregular manner, and this had led to the formation of irregular masses and tracts of cells. The hard portions of the tumour were composed of very coarse primitive fibrils and fibril bundles which were infiltrated with lime salts. Other parts contained all the osseous elements of bone, corpuscles, Haversian canals, concentric lamellæ and cellular marrow spaces.

Where the tumour was fused with the floor of the third ventricle there was a loose œdematous connective tissue with numerous coarse and delicate wavy fibres forming a wide-meshed reticulum. Dorsal to it was seen a portion of the choroid plexus, the ependymal cells of which had proliferated and formed branching villous excrescences. No cartilage was found in the tumour nor any glia cells or fibres. Hecht regarded this tumour as belonging to that type of teratoma which imitates an entire embryonic region.

The other tumours similar in structure to those of Cases 1 and 2, and which the writers regarded as having possibly originated from the third ventricle, were described by Lereboullet, Morizon and Cathala [11], and the other by Claude and Schaeffer [1]. Cushing [2], Wilfred Harris and Cecil Graham [6], have also recorded cases of cystic epitheliomata of the infundibulum and third ventricle.

Erdheim [3] in 1904 described seven personally observed cases of tumour which he considered to have arisen from "rests" of that part of the ectoderm of the original embryonic buccal cavity which goes to form the cranio-pharyngeal duct. A part of this lies during its final development in the region of the infundibulum and the upper surface of the anterior lobe of the pituitary, and he demonstrated the frequency with which "rests" of the duct occur in this situation by finding them in ten out of thirteen fœtuses examined. These tumours are described as being always in the mid-line and generally originating in the infundibulum. Some were solid but the greater number were cystic and contained a serous fluid in which cholesterin crystals were frequently found. The tumour tissue is described as being epithelial and the cells as resembling those of the buccal mucosa. Both macroscopically and microscopically these tumours appear to resemble very closely the first two described above. Various other observers have followed Erdheim in considering such epithelial tumours to have been derived from the cranio-pharyngeal duct, basing their conclusion partly on the structure of the tumour and partly on its situation.

One of the most striking examples was that described by Farnell [4]. This was a tumour about the size of a golf-ball occurring in the usual situation, in the mid-line and behind the optic chiasma. It had an adeno-papillomatous structure. The remarkable feature of the tumour was that the epithelial tissue not only resembled the buccal epithelium, but even the mandibular type of epithelium composing the enamel-forming organ of the tooth. Hence Farnell regards the tumour not only as a hypophyseal cholesteatoma, but also as an adamantinoma comparable to the tumours which develop in the jaw from the dental epithelium. All these cranio-pharyngeal tumours, however, do not present such a typical form of epithelioma. Many of them have been described as being papillomatous, with flat-celled epithelium, and sometimes as containing apparently isolated cell-nests. They thus resemble very closely the structure of the tumours of the first two cases described in this paper. Such neoplasms have also been reported by Harms [5], Kankeleit [9], Mackay and Bruce [14], Strada [18], Lewis [12], and Harry Jackson [8].

The cyst in Case 3, the wall of which contained only fibrous tissue, is evidently of a rarer type. Except that it apparently originated from the infundibulum, its origin is obscure.

There is no doubt that growths of an epithelial nature are the most frequent type of supra-pituitary tumour. Other types of tumours which have occurred in this region are two instances of teratomata and one of an endothelioma described by Cushing [2]. Lockwood [13] records a typical cholesteatoma, Silfvast [17] a glioma and an endothelioma. A case of myxo-chondro-sarcoma was published by Mott and Barratt [15], who also report a very rare instance of mycotic infection which, by irritation, had set up a new growth in the supra-pituitary region.

These tumours occurring in the supra-pituitary region generally produce fairly constant local and general symptoms. The chief local symptoms are those due to involvement of the chiasma and optic tracts, generally producing a bitemporal hemianopsia, and eventually total blindness with optic atrophy if the tumour is not partially removed by operation. In a late stage of the disease there is often increased intracranial pressure, brought about mainly by interference with the escape of cerebrospinal fluid from the lateral and third ventricles. The general symptoms, however, are much more interesting ; they generally approximate to the type of dystrophia adiposo-genitalis described originally by Fröhlich. The outstanding symptoms are adiposity, with a feminine type of fat distribution over chest, abdomen, hips and pubes, and either non-development of the secondary sex characteristics if the condition had occurred before puberty, or some loss of them if the condition had commenced after puberty. Hence in cases in which the disease begins in childhood, the genital organs always remain infantile; the pubic and axillary hair never becomes more than very scanty, and in girls menstruation is never established. When the condition sets in after puberty has been established, cessation of menstruation in women and impotence in men are early symptoms, and the genital organs gradually revert back to pre-adolescent state. There is a very decided diminution in the body hair; the axillary hair often disappears altogether, that over the pubes becomes very scanty. The beard and moustache become thin, or the patient may not need to shave so frequently as previously, although the hair of the scalp does not seem to be affected. The skin of these patients is generally very dry, and extremely smooth and delicate. Metabolism is often, though not always, deranged. Frequently there is an increased carbohydrate tolerance. In other cases, such as those reported by Newmark [16] and by Cushing [2], an outstanding feature was diabetes insipidus. Low blood-pressure, epileptiform seizures, and lowered mentality may also occur. The cause of these striking symptoms has been the subject of much investigation. On account of the involvement of the pituitary gland by pressure of these supra-pituitary tumours, the symptoms have been generally attributed to a diminished secretion of the hypophysis. This theory of hypopituitarism as the cause of Fröhlich's syndrome has been strongly supported by the experiments by Cushing upon dogs. He found that puppies deprived of all their pituitary gland, except a fragment of the pars anterior, became adipose, their sugar tolerance was increased, they remained sexually infantile, and skeletal growth was very greatly retarded. Similar experiments upon adult dogs produced adiposity, increased sugar tolerance, and reversive sexual changes. Further, he observed that animals deprived of only the posterior lobe of the pituitary gland acquired a high sugar tolerance and became very fat, and that intravenous injection of posterior lobe extract produced glycogenlysis, and its continued administration in excessive amounts leads to emaciation.

The exact relation of polyuria and polydipsia to the pituitary gland is still somewhat uncertain, but its occasional occurrence in tumours in the pituitary region indicate that the relation is a close one. Newmark [16] has described a case of severe diabetes insipidus, in which a tumour occupying the region of the infundibulum was found to have destroyed the pars nervosa and most of the pars intermedia. The second case described in this paper had polyuria. It would, therefore, appear as if a destructive lesion of the pars nervosa might result in polyuria. On the other hand, the oral administration of posterior lobe substance in animals had been observed by Schäfer to have a diuretic effect.

There is, therefore, much evidence correlating the state of dystrophia adiposo-genitalis presented by cases of supra-pituitary tumour with the damage or destruction of the gland. It is also possible that the normal discharge of the posterior lobe secretion into the third ventricle via the infundibular cavity may be interrupted by the involvement of the infundibulum by the tumour. On the other hand, Erdheim believes that the Fröhlich syndrome may be caused by the growing tumour interfering with certain centres at the base of the brain apart from the pituitary gland.

A perusal of the literature on the subject of supra-pituitary tumours shows that about 70 per cent. of these tumours are associated with Fröhlich's syndrome.

The writer is indebted to Dr. Gordon Holmes and Dr. Farquhar Buzzard for permission to publish their cases, and to Dr. Godwin Greenfield for taking the photographs which illustrate this paper.

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THE NERVOUS CONTROL OF THE URINARY BLADDER IN AMPHIBIANS.[1]

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THE experiments described in this paper were undertaken to determine whether the normal evacuation of the urinary bladder in amphibians depended on the integrity of some part of the anterior end of the hind-brain, as has previously been shown to be the case in the cat [1].

The animals used were the common frog (*Rana fusca*), the common toad (*Bufo vulgaris*), the crested newt (*Molge cristata*) and the spotted salamander (*Salamandra maculosa*).

Various proportions of chloroform and ether dissolved in water were tried for the anæsthetic. One c.c. of ether to 100 c.c. of water appeared to be the best, and this mixture was used in the majority of the experiments. The animals were put in a closed glass vessel containing such a quantity of this mixture that they were not completely submerged, and left there till all reflexes, including respiration, were abolished. Though given no further anæsthetic they did not come round till a considerable time after the operation was finished.

After operation the animals were kept till they were killed in a sink into which water was slowly dripping; the surface of the sink was therefore always wet but there was not sufficient water in it to cover them. Most of the animals were kept two days after operation; they were then killed with ether water, the abdomen opened and the degree of distension of the bladder noted. This can easily be determined in frogs during life by a translucent area in the region of the bladder; the same applies to the other animals if a strong light is used. From the observations it seems that two days was an unnecessarily long time, and probably the same results would have been obtained if the period had been one day.

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[1] The expenses of this research have been defrayed by a grant from the Dixon Fund of the University of London.

THE EFFECT OF REMOVAL OF PARTS OF THE BRAIN.

Portions of the brain were removed in anæsthetized animals by removing part of the roof of the skull, dividing the brain transversely and scooping out the part anterior to the section; the skin incision was then closed. The actual position of the brain transection was determined after death and hardening in formalin by naked-eye examination.

These experiments were made on fourteen frogs, length between 5 and 7 cm.; five toads, length between $6\frac{1}{2}$ cm. and 9 cm.; eight newts, length between $11\frac{1}{2}$ cm. and $14\frac{1}{2}$ cm.; and eleven salamanders, length between $11\frac{1}{2}$ cm. and $15\frac{1}{2}$ cm.

When killed the animals fell into two groups according to the appearance of the bladder; in the one it was tensely distended and marked abdominal distension was present, and in the other, even though containing a considerable amount of urine, its surface always had a crenated appearance; in no case was there ever the slightest doubt into which of these two groups to place an individual animal. Measurements of the bladder contents, though unnecessary, were in most cases attempted by delivering the bladder through an abdominal incision and opening it over a measure. In the case of the frog the figures obtained by this method probably give a fairly accurate idea of the degree of distension. In the toad and salamander the figures usually represent less than the actual degree of distension in the case of distended bladders, since in opening the abdomen a large amount of fluid often escapes from the cloaca. This appears to be due to the absence of a lax skin like that of the frog. In the newt the bladder is so small that the drops adhering to the opened bladder, sides of the measure, &c., may form an appreciable proportion of the bladder contents. In the frogs the normal maximum quantity of urine that can be collected in this way is probably under 2 c.c.; the amounts collected in those with over-distended bladders varied from $3\frac{1}{4}$ c.c. to 12 c.c. In the toad the normal maximum appears to be up to 10 c.c.; the amounts collected in those with over-distended bladders varied from 10 c.c. to 59 c.c., in the former a considerable quantity was known to have been lost. In the newt the quantities collected from those with over-distended bladders varied from 0·3 c.c. to 1·2 c.c., and in the salamander from $3\frac{1}{2}$ c.c. to $11\frac{1}{2}$ c.c.

Removal of the fore-brain only, with one exception, was never followed by an over-distended bladder; the exception was a salamander and after hardening the mid-brain was found to have become softened. In all cases where the transection was behind the cerebellum an over-distended bladder resulted. With the exception of one newt, on which not much reliance can be placed on account of the small size of the brain, all cases where the transection went between the cerebellum and the mid-brain resulted in an over-distended bladder. With the exception of one frog in which the whole mid-brain was found to be softened, no experiment resulted in an over-distended bladder where the transection was made through the anterior half of the mid-brain. A transection through the posterior half of the mid-brain was only made in one frog and in it the bladder was not over-distended. If therefore, as is probable, the result in the newt alluded to was an error in observation, the over-distended state of the bladder observed in all four species is due to the destruction of some part of the posterior half of mid-brain.

This localization approximates to that already described in the cat as nearly as could be expected from the methods employed in the two cases. In the cat, however, paralysis of the bladder was shown to be present; in the amphibian the over-distension might be due to this or to failure of the closing mechanism to relax. A third possibility arises from the fact that the ureters do not open directly into the bladder, namely, that the over-distension might be due to some abnormal rate of filling of the bladder. This, however, cannot be the explanation, since in normal frogs it is quite easy to see that the bladder is emptied when urine is passed by the disappearance of the translucent area in the bladder region, whereas in animals with over-distended bladders, even though considerable quantities of urine may escape during struggling when the animal is handled, a large translucent area in the bladder region persists. Though there is no direct proof that the failure of the bladder to empty is due to its paralysis, it seems unlikely that it is dependent on a tonic contraction of the sphincter from the fact already stated that in animals with over-distended bladders comparatively slight mechanical causes can lead to the expulsion of considerable quantities of urine from the cloaca, though the bladder is still over-distended at the end.

THE EFFECT OF DIVISION OF THE SPINAL CORD AND OF THE SPINAL ROOTS.

(*a*) *In the Anura.*

Division of the spinal cord in frogs, the species of which is not stated, was found by Exner [3] to lead to great dilatation of the bladder; the level of transection was stated to be at the fourth or fifth vertebra, but it is not given in relation to spinal roots. It was shown by Gaskell [4] that the bladder of the frog, as of the mammal, has a double innervation, the anterior fibres reaching it by the sympathetic and the posterior, which correspond to the pelvic nerve of mammals, arising directly from the sciatic plexus. The spinal roots from which contraction of the bladder could be elicited in the frog were found by Horton Smith [5] to be the ventral roots of the seventh, ninth and tenth, but not of the eighth; the seventh required a stronger stimulus to obtain the effect than the ninth or tenth. Dale [2] showed that in the toad stimulation of the same roots, the seventh, ninth and tenth, and of these only, gave rise to contraction of the bladder.

In the experiment about to be described the first root is considered to be the one emerging between the first and second vertebræ. In many experiments on frogs and toads the lower roots are counted from the posterior end and errors are therefore liable to occur if there is a variation of the normal root arrangement. In the urodela the levels of lesions are given in vertebræ; as the roots emerge from the spinal canal directly they arise from the cord this is not open to objection.

Division of the spinal cord at various levels from the second to fifth roots was performed in six frogs and four toads; in some experiments the cord posterior to the transection was excised, in some it softened and in others it functioned, reflex movements of the hind limbs being obtainable. In all these cases great over-distension of the bladder resulted. The nervous impulse which leads to the normal emptying of the bladder must therefore travel from the posterior half of the mid-brain down the anterior half of the spinal cord.

In two frogs the cord was divided behind the seventh roots and no abnormal distension of the bladder occurred. Division of the ninth and tenth spinal roots was performed in three frogs and five toads; over-distension of the bladder did not result in any case. The toads usually had full bladders when killed but they were always within the normal limits: in the three frogs the bladders were nearly or quite empty. At any rate the whole mid-brain effect cannot act through the posterior spinal nerves. This appeared such a fundamental difference from the condition in the cat that it was thought the mid-brain influence might be masked by a possible paralysis of the sphincter of the bladder. This was shown not to be the case by dividing the ninth and tenth roots and the cord between the second and third roots at the same operation: flexion of the hips and knees could be obtained then by touching the toes and an over-distended bladder resulted.

Division of the lower spinal roots, excepting the last two, is a difficult operation in the frog and toad, and not an easy one to control by dissection two days after it has been done. It was attempted by removing the laminæ of the four hindmost vertebræ and dividing all roots exposed which emerged in front of the ninth vertebra on both sides. In this way the sixth, seventh and eighth roots were usually divided and the ninth and tenth left intact. In three frogs there was over-distension of the bladder after this operation, but in these there was complete paralysis of all movements of the limbs, including the toes: the ninth and tenth roots, though not actually divided, were therefore not functioning. In one frog in which this operation had been performed, and the ninth and tenth roots of one side divided as well, there was no over-distension of the bladder, but voluntary flexion of the toes of the opposite side occurred during life. In two other frogs, where the sixth, seventh and eighth roots had been divided on both sides, there was no over-distension of the bladder; movement of the toes was seen in one, but in the other no observations were made on this point. In two other frogs the seventh root on both sides, and the seventh and eighth on both sides, were divided and no over-distension of the bladder resulted. Division of the seventh root in frogs does not, therefore, lead to over-distension of the bladder if the ninth and tenth roots are intact even on one side. One experiment only was an exception to this, and does not seem easy to explain: an over-distended (8 c.c.) bladder was present in a frog: anatomical examination showed the ninth and tenth roots intact, and the sixth and seventh roots divided on both sides, the eighth root was intact on the right side, and its dorsal part only divided on the left side: during life there was paralysis of the whole left hind limb except for movement of the toes, but flexion of all joints of the right hind limb occurred. The sixth, seventh and eighth roots were divided in one toad: paralysis of both hind limbs except of the toe movements resulted, but there was no over-distension of the bladder.

In the frog and toad, therefore, both the anterior and posterior sets of roots must be divided to produce over-distension of the bladder; from this it follows that the impulses from the posterior part of the mid-brain which normally prevent over-distension must pass out through both sets of nerves.

(b) *In the Urodela.*

In two newts division of the cord at the eighth and at the tenth vertebræ respectively resulted in an over-distended bladder.

The nerve roots supplying the bladder in the salamander are apparently not known. Only one experiment was made on this animal. The brain having been destroyed, the laminæ of the eleventh to the eighteenth vertebræ were removed; the cord was damaged in doing this, and it was divided at the level of the twelfth vertebra. It was then stimulated with a unipolar electrode at the posterior border of each vertebra, from the twelfth to the eighteenth inclusive, for about ten seconds; contraction of the bladder occurred when the stimulus was applied at the lower border of the seventeenth vertebra but nowhere else. An attempt was then made to divide this part of the cord into segments and the stimulation repeated with the same current (Kr. 400); the contraction again only occurred at the seventeenth. The stimulus was then increased and the experiment repeated twice again; a marked bladder contraction resulted at the seventeenth vertebra on both occasions and a doubtful one at the fifteenth on one. In this salamander the large roots to the hind limb plexus were the fifteenth, sixteenth and seventeenth; the seventeenth root therefore corresponds to the ninth in the frog and toad. The experiment does not show whether an upper set of nerves exists, and if so where it is, but it is sufficient to show the main part of the lower set arises from the posterior part of the hind limb plexus as in the frog, toad and mammal.

In three salamanders the cord was divided and in all an over-distended bladder resulted. In one the level of transection was the fifteenth roots, the fourteenth being the most anterior large root to the hind limb plexus. In the other two the level was the sixteenth root, and the fifteenth and sixteenth respectively were the first large roots to the hind limb plexuses. It is therefore probable that if an upper set of bladder nerves exists in the salamander only the lower set convey impulses from the posterior part of the mid-brain to the bladder, in which case the salamander differs from the frog and toad in this respect and resembles the cat.

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Proceedings of the Section of Neurology of the Royal Society of Medicine.

President—Mr. PERCY SARGENT, C.M.G., D.S.O., F.R.C.S.

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Some Varieties of Traumatic and Toxic Ulnar Neuritis.

By E. FARQUHAR BUZZARD.

MY interest in the ulnar nerve was first excited in a very personal manner about twenty-five years ago. Having succeeded during the course of a hospital football match in fracturing one of my collar bones, my arm was duly fastened to my chest in a position of extreme flexion at the elbow with results which still live vividly in my memory. After a very few hours I began to experience discomfort in the sensory distribution of the ulnar nerve. At the end of a couple of days the pain and paræsthesia were so intense that I was obliged to beg for the release of my arm from its fixed position. It is quite true that many persons are able to submit to the same procedure without experiencing any discomfort, and it would seem that some anatomical peculiarity was responsible for my distress. At the same time this peculiarity is shared by a good many people, some of whom complain that if they sleep with an arm flexed, they are liable to wake with paræsthesia referred to the distribution of the ulnar nerve.

NEURITIS WITH NO OBVIOUS ANATOMICAL FEATURE.

With this introduction I may refer at once to the first group of cases of ulnar neuritis to which I would like to draw your attention. In this group there is no obvious anatomical feature which can be regarded as a factor in the production of the neuritis. Examination of the nerve at the elbow does not reveal any abnormality in regard to its relations with bony structures, and it lies well protected in the ulnar groove. The complaint may be limited to a transient disturbance of function as a result of the excessive use of the hand and arm in a flexed position. A good example of this was the case of a lady, aged 33, who complained of complete failure of function on the part of the two ulnar fingers of the left hand occurring on several occasions at the end of a long 'cello recital. She had played the 'cello since she was 5 years of age, and had recently indulged in what may be regarded as excessive hours of practice. But it is possible to produce more permanent ulnar disturbances by excessive use of an arm, as in the case of a man who came to me complaining of numbness in the ulnar fingers of the right hand and slight pain in the region of the elbow. On examination, there was found some loss of epicritic sensibility in the ulnar distribution and slight atrophy and weakness of the ulnar muscles, including flexor carpi ulnaris. At the elbow the nerve seemed to be in good position, and the only abnormality found was slight tenderness just below its exit from the ulnar groove. This condition had apparently been produced by a long spell of fishing with a heavy salmon rod, and any attempt at using a rod or a tennis racket sufficed to renew the pain, and was attended with difficulty in maintaining a proper grasp.

Even less violent exertions may sometimes end in a similar condition. For instance, a lady, aged 43, complained that for three weeks she had had difficulty in using her right hand, and was conscious of a pain like a sting in the ulnar border of the palm and in the two ulnar fingers. The ulnar muscles were obviously weak, but showed very little atrophy, and no definite sensory loss could be detected. The only ætiological factor which I could discover in her case was a period of excessive use of the hand in sewing and writing.

Cases with an Additional Toxic Factor.

Closely allied to the group I have just described is another in which it is possible to find an additional ætiological factor in the form of some toxic agent. In these cases, again, no anatomical abnormalities can be detected, and the most characteristic feature of this form of ulnar neuritis is its onset, while the patient is confined to bed with some infective or septic illness. I saw quite a number of cases of this description during the war, especially among soldiers confined to bed with severe compound fractures and subsequent prolonged sepsis.

Captain G. M., aged 21, sustained a wound of the right leg, which was amputated. He was laid up for three months in bed with septic complications, and after about two or three weeks noticed increasing numbness and soreness in the ulnar fingers of both hands. The right hand recovered in the course of five weeks, but the left hand showed atrophic palsy of the ulnar muscles, with some sensory impairment in the ulnar cutaneous area.

I am inclined to attribute the ulnar neuritis in these cases partly to the fact that the arms are constantly being used in the flexed position—partly, perhaps, to an undue amount of friction, and partly to the effect of some toxic agent. In civilian life I have seen a precisely similar condition arising bilaterally in a patient who had been in bed for a fortnight with a slight attack of small-pox. All the cases of this kind which I have come across have made a good recovery. Perhaps one ought to include in this group the occasional case of ulnar neuritis associated with glycosuria, and others in which the only ætiological factor of importance appears to be the gouty diathesis. An interesting example of the latter was a patient, aged 61, who came to me complaining of pain in the ulnar fingers and ulnar aspect of the left hand which had come on suddenly eight months previously after sitting out one evening in the garden. I found definite, but slight, wasting of the ulnar muscles and slight impairment of sensibility in the ulnar area. He suffered from gouty eczema, a gouty big toe, and presented gouty deposits in the lobe of the left ear.

Cases with Some Anatomical Peculiarity.

My third group of cases comprises those in which some anatomical peculiarity can be discovered in connection with the relations of the nerve at the elbow. These cases may be subdivided into: (1) those with a history of severe injury to the elbow; (2) those without any history of trauma.

(1) It has long been recognized that ulnar neuritis may develop many years after an injury to the elbow, and this condition has been ascribed to involvement of the nerve in callus or in fibrous adhesions. I have seen a number of cases of this kind, and the outstanding feature has always been the unprotected position of the nerve at the elbow. It would seem that in these cases the nerve is constantly exposed to minor insults and injuries, each one of which may produce very little immediate effect, but which in the aggregate lead to the formation of a fibrous neuroma. This neuroma is generally a fusiform swelling of the nerve due to a large increase of its connective tissue elements. I have never found any evidence of bony pressure, and fibrous adhesions to neighbouring structures are rarely prominent. On the other hand, some fibrous constriction of the nerve is not very uncommon.

Mrs. O., aged 30, gave me a history that two and a half years before our interview she had sustained a violent blow on the right elbow with a tennis racket and that some months later she began to find slight difficulty with her right hand. She was unable to play tennis or use the arm in any strenuous way during the following summer. She complained of pain in the elbow even when writing or using a needle, and I found the nerve at the elbow very easily displaced and over-exposed. It was tender on palpation and there was some impairment of sensibility in its distribution. Mr. Wilfred Trotter placed this nerve in front of the joint in March, 1920, with the result that the patient is now able to use her hand and arm without any discomfort or disability.

Mrs. S., aged 45, gave a five years' history of wasting and weakness of the left hand with slight pain at the left elbow and in the ulnar side of the hand. She displayed almost complete ulnar palsy as regards the intrinsic hand muscles and some weakness of flexor carpi ulnaris. There was only slight sensory disturbance. The nerve at the elbow was thickened and exposed. In this case there was a history of fracture of the left arm at the elbow forty-two years previously. Mr. Trotter operated and found a spindle-shaped neuroma of the nerve at the elbow, and contented himself with transposing it in front of the joint.

(2) There appear to be a number of people whom nature has treated rather shabbily in regard to protection of the ulnar nerve at the elbow. The groove is very shallow, and when the elbow is passively flexed the nerve can be felt to slip out of it and to lie in an exposed position over the inner condyle. These people may escape any serious consequences of their anatomical peculiarity unless circumstances necessitate a more or less strenuous and continued employment of their arms.

A very good example of this type of case was provided by a man, aged 46, who was sent to me complaining of weakness and wasting in the left hand, and with a sensation of numbness on its ulnar side during a period of about four months. On examination I found a very poor ulnar groove and a large thickened nerve easily palpable on the surface of the bone; there was almost complete atrophic palsy of the ulnar muscles, including flexor carpi ulnaris, and partial sensory loss in the ulnar distribution.

The chief exciting factor in this case appeared to be the fact that the patient spent his time driving a two-horse van with his left arm. A possible accessory factor may have been a somewhat excessive consumption of beer. Mr. P. Sargent operated on this patient and found a fusiform swelling involving the whole thickness of the nerve for about three-quarters of an inch. Below this neuroma the nerve passed beneath a dense fibrous archway which constricted it.

I have seen many other cases of this kind, and a particularly interesting example was the following :—

A platelayer was in the habit of swinging a heavy hammer impartially with both arms. When I saw him he was complaining of atrophy and weakness of the muscles of both hands characteristic of an ulnar lesion. Both ulnar nerves were unusually unprotected and mobile at the bend of the elbows and each exhibited a large diffuse neuroma.

This case afforded a good example of difficulty in diagnosis in that he complained of no pain and but little paræsthesia in his hands. Except for the limitation of the atrophy to the muscles supplied by both ulnar nerves, he would have passed for a case of progressive muscular atrophy, the diagnosis with which he arrived in my out-patient room. It is worthy of note that the sensory disturbance in these patients varies very much, but on the whole is less severe than the motor palsy and muscular atrophy.

Differential Diagnosis.

A careful examination should suffice in all cases to distinguish an ulnar palsy from a spinal cord lesion in the form of progressive muscular atrophy or syringomyelia. On the other hand, so much attention has been paid in recent years to the presence of cervical ribs and the interesting clinical phenomena to which they give rise, that cases of the kind I have been describing are not infrequently sent for X-ray examination on the suspicion that a supernumerary rib may be held responsible for the disability. That such a procedure may give rise to confusion rather than to help in diagnosis is well illustrated by a patient whom I saw two or three years ago and who was ultimately operated on by my colleague, Mr. Cyril Nitch.

He was a man 40 years of age, who, seven years before he came under observation, fell off a motor bicycle and injured his right elbow. He was told that there was no fracture of the bone, but the joint was painful for several weeks and for some time he was unable to straighten his arm. He made a complete recovery, but six or seven years later he noticed wasting of some of his right hand muscles and he felt an occasional tingling over the ulnar side of his hand on straightening his arm. This wasting was preceded for a time by a condition of cramp in his fingers when he was writing. On examination there was distinct wasting of the first dorsal interosseous muscle and epicritic sensibility over the ulnar border of the hand was diminished. The ulnar nerve at the bend of the elbow was freely movable and not obviously thickened. This patient had both his elbow and neck X-rayed. The skiagram of the elbow showed an old fracture of the external condyle with downward displacement, but no signs of injury to the internal condyle. The skiagram of the neck revealed a well-developed seventh cervical transverse process on each side and a rudimentary cervical rib on the right. The motor and sensory disturbance in the hand determined the diagnosis in spite of the cervical rib, and Mr. Nitch exposed the ulnar nerve at the back of the elbow. It was much thickened by scar tissue in the groove behind the internal condyle and was bound down to the latter by firm adhesions attached to its sheath. On palpation the nerve felt tough and fibrous. It was lifted from its bed after dividing the fascia uniting the two heads of flexor carpi ulnaris and was displaced forwards in front of the internal condyle and kept in position by a graft of subcutaneous fat. Within a few weeks the patient had lost all sensory disturbance, and he returned to his work in the East with the intention of continuing electrical treatment to the wasted muscles.

The number of cases which I have very briefly outlined suggests that the ulnar nerve is particularly prone to disturbances of function on what appear to be at first sight slight provocation. Looking for a common factor in these various groups one is struck by the fact that in the majority of cases the ulnar nerve is unprotected by any bony parapet at the bend of the elbow, or so badly protected that during extension and flexion of that joint it is apt to slip in and out of its proper position. During flexion especially it may lie exposed to friction and pressure on the internal condyle. A consideration of many cases seems to justify the conclusion that movement, especially of a strenuous and frequently repeated character, is an important factor in the production of an interstitial neuritis. This moving contact with a bony surface is probably an important factor in producing the symptoms associated with a cervical rib, although I do not think it has been shown that in the latter case the nervous tissue becomes surrounded by a definite thickening of connective tissue. In the case of the ulnar nerve, however, the nervous tissue is constantly exposed to minor injuries, and the neuromatous condition so often found must be ascribed to chronic inflammation of traumatic origin. It is a little difficult to understand why the flexed position of the elbow should in itself give rise to discomfort referred to the distribution of the ulnar nerve, as I believe there is no evidence to show that the nerve is stretched by that posture of the limb.

DISCUSSION.

Dr. WILFRED HARRIS said he also had a peculiar interest in the ulnar nerve since the time when, as a schoolboy of 13 years, his left ulnar nerve was struck at the elbow by a stone thrown by another boy. He had great pain at the time and had constantly received minor injuries to his ulnar nerve ever since. He thought that this was one of the disadvantages of the erect position of man, since this posture necessitates frequent acute flexion at the elbow and stretching of the ulnar nerve. In some of the carnivora the ulnar nerve passes forwards into the forearm through a foramen in the lower portion of the humerus above the joint and is thereby less subject to stretching. There was one point in the distribution of the ulnar nerve which he wished to emphasize. In some cases the ulnar nerve did not supply the first and second dorsal interossei, and in such cases, unless this possibility were realized, a peripheral ulnar lesion might easily be mistaken for a central one.

Dr. STANLEY BARNES emphasized the nervous origin of the various occupational muscular atrophies. He saw many such cases in his practice in a large industrial centre ; some of them exhibited swellings on the nerve trunks. He instanced one case where a lad, now 17 years old, suffered from a severe ulnar neuritis due to a fracture of the internal condyle of the humerus when he was 7 years old. The nerve could be felt running over a promontory, instead of being in a groove. It was difficult to know what to do for this case ; every possible measure had been tried except operation, and Dr. Barnes' war experience of resection and suture was not sufficiently encouraging to justify such treatment so long as any muscular power or sensation remained. Occupational neuritis of the ulnar nerve was due in many cases to friction between the nerve and the humerus due to prolonged use of the arm with the forearm flexed. In a few cases he believed that friction occurred higher up between the clavicle and the first rib.

Dr. G. RIDDOCH said that the pain resulting from ulnar neuritis due to bone injury could hardly be connected with the involvement of nerve in callus, since it appeared so very late. He instanced a case where the pain came on fifteen months after the injury. This case had proved very difficult to treat. Alcohol injection of the nerve had given relief for one month, and a recent surgical operation had resulted in complete relief for three weeks, but the symptoms were now beginning to reappear. Dr. Riddoch also commented on the fact that some patients exhibited motor and others sensory symptoms following the same sort of injury.

Dr. HENRY HEAD quoted Mr. Sherren's paper on "Neuritis of the Ulnar Nerve, due to Deformity in the Region of the Elbow-joint" (*Edin. Med. Journ.*, June, 1908). In one of these patients the neuroma was excised, the two ends of the nerve sutured, and a fresh groove chiselled in the back of the internal condyle. Voluntary power began to return in sixty-six weeks and all the muscles acted voluntarily in one hundred and thirty-two weeks. Sensibility was also restored. To-day it would be better in such cases to displace the nerve to the front of the internal condyle. Dr. Head also pointed out that the protopathic supply of the ulnar nerve extended on to the median half of the palm. This was shown by irritative lesions and could be demonstrated in normal persons by applying a faradic current to the ulnar nerve at the elbow ; painful tingling extended across the palm almost to the root of the thumb. On the other hand, division of the ulnar caused loss of sensibility over that area alone assigned in the text-books to this nerve.

The PRESIDENT referred to the delay in the appearance of symptoms after fracture of the lower end of the humerus. He had seen a clerk, aged 30 years, whose recent ulnar neuritis could only be attributed to a fracture at the age of 4 years. A variety of pathological conditions might be found in these cases. Adhesions were often a cloak for ignorance, but he had in one instance seen a case where the nerve had been compressed under the fibrous arch between the two heads of the flexor carpi ulnaris; complete relief had followed the division of this arch. In another extraordinary case, that of a carpenter who could not flex the elbow beyond a right angle without pain, the nerve was found to be normal at operation, but a loose cartilage was found in a synovial pouch lying between the nerve and olecranon process. The removal of this cartilage cured the patient. For the ordinary type of neuritis associated with a fusiform neuroma, it was his practice to make longitudinal incisions in the sheath, and to transplant the nerve in front of the arm. He agreed that resection of the neuroma with suture of the nerve was quite unnecessary in these cases.

Dr. BUZZARD said he had noticed the occasional abnormal distribution of the ulnar nerve first described by Dr. Harris. The post-traumatic cases could not be due to callus formation, but were due to the more exposed situation of the nerve which resulted from the obliteration of the groove in which it was normally protected, and to the increased amount of movement which resulted from this.

NOTICES OF RECENT PUBLICATIONS

Die Vergleichende Anatomie des Nervensystems der Wirbeltiere und des Menschen. By Dr. C. U. ARIËNS KAPPERS. II Abschnitt. Mit 320 Figuren im Text und 7 Tafeln. Pp. 705. Haarlem: Bohn. 1921.

The first volume of this book, which was reviewed in a recent number of this Journal, has been quickly followed by the publication of the second and concluding part. Kappers' Comparative Anatomy of the Nervous System of Vertebrates and Man is now complete, and certainly stands without any rival as to the most comprehensive, authoritative and up-to-date textbook on the subject. Lest its title suggest to clinical neurologists and others that it is merely a comparative anatomy and is concerned exclusively with subjects of less immediate interest to them, it must be pointed out that there are few books in which the anatomy of the human brain is so thoroughly and intelligently dealt with.

The first chapter is devoted to the cerebellum, the development of which is traced upwards from its first appearance in petromyzon, where it is merely a correlation centre between the vestibulo-lateral apparatus and more frontally situated mechanisms, to man. Its subdivision, adopted by Kappers, is based largely on the work of his pupil Ingvar, and consequently differs in certain respects from that of Bolk, Elliott Smith and other anatomists, though it is in principle closely allied to them. According to this view the neo-cerebellar parts, to which its increase in size in the higher vertebrates is due, develop in connection with the lobus medius, that part of the vermis which lies between the sulcus primarius and sulcus præpyramidalis, as a result of newly acquired connections with the inferior olives and with the cerebral cortex through the pontine grey matter; while the palæocerebellar components, including the lobus anterior, lobus posterior and formatio vermicularis, remain fundamentally unaltered. An interesting section is devoted to the question of functional localization in the cerebellum, in which the matter is considered from the physiological and experimental as well as from the anatomical point of view.

In the following chapters the midbrain, thalamencephalon, rhinencephalon, corpus striatum and neopallium are dealt with in the same method. One of the most interesting and instructive of these chapters is that which describes the evolution of the corpus striatum and the development of its connections. By following, as the author does, its growth in the succeeding genera of vertebrates, we are enabled to understand not only the rôle it plays in the evolution of the brain, but also the significance of its separate parts and their multifarious and complex connections. This chapter is certainly not easy reading, but the student who masters it will obtain a better knowledge of the basal ganglia than he can hope to do by any other method of study.

The final chapter is devoted to the neopallium. Here the comparative method has less scope, but the comparison of the different parts of the cerebrum in different genera, and a study of the stages through which each has passed before attaining its final form in the highest vertebrates, throws so much light on structures which we ordinarily know only from a study of human anatomy that we cannot but be grateful to the author for the opportunity which he gives us here of reviewing them in a compact and very readable form.

The volume under review is as copiously illustrated as the first; there are 320 figures scattered through its 705 pages, and in addition seven coloured tables. Specially valuable features of both volumes are the comprehensive bibliographies at the end of each chapter, and the very complete index of subjects and names.

Die neurologische Forschungsrichtung in der Psychopathologie, und andere Aufsätze. By Dr. A. Pick. With 11 Figures in the Text. Pp. 247. Berlin: Karger. 1921.

Throughout a long and fruitful life Professor Pick has always been interested in phenomena which illustrate the relation of mind and body. Such questions as the nature and causes ot aphasia, apraxia, katatonia and hallucinations associated with lesions of the brain, have been his constant preoccupation. As one of the few writers on the Continent who have assimilated and understood the doctrines of Hughlings Jackson, he looked upon these mental changes as dissolutions of highly integrated functions and pointed out in what instances they revealed the activity of lower centres, normally kept under control. This he calls the "Neurological attitude in psycho-pathology."

The first 93 pages of his book are taken up with an essay on the value to mental medicine of the psychical changes evoked by organic nervous disease, and all the subsequent pages form examples of this method of approach. Motor and static perseveration are brought into relation with katatonia; apraxia is explained by the work of Leyton and Sherrington on the cortex, and the somewhat similar views of von Monakow are shortly discussed.

The next paper deals with the pathology of linear writing, based on a case of eclamptic psychosis. This is followed by a consideration of the exceptions to Ribot's law, that in disorders of speech the most recent acquisitions, e.g., a foreign language, are first affected. Pick then discusses the psychology of recurrent utterances in aphasia and passes on to deal with what the French have called "palilalie" or multiple repetitions. This he believes to be associated particularly with lesions of the basal ganglia.

The last paper is a description of visual hallucinations, which followed local treatment to his own eye, after the lens had been extracted for cataract. These took the form of letters projected on some surface at a distance, such as the blind, or the cheek of the person to whom he was talking. When they appeared on a dark surface, they were surrounded by a luminous background. Such obscure phenomena already possesses a considerable and little known literature: this has been collected with the author's well-known care and thoroughness.

Der Balken. By G. MINGAZZINI. Pp. 212. Berlin: Julius Springer. 1922. M. 160.

This, the latest contribution to the series of monographs edited by Foerster and Wilmanns, is an interesting and instructive book which certainly attains the high level of the preceding volumes of the series. In successive sections the author deals with the anatomy and development of the corpus callosum, and with the symptoms which result from its destruction by vascular lesions and tumours, and from its degeneration due to other causes. Finally he discusses its function, especially from the clinical point of view, and points out the important part affections of it may play in the determination of defect phenomena in man. His general conclusion is that the corpus callosum is concerned in the eupraxia of the limbs, especially of the upper extremities; in the integration of spatial perceptions; and in the correlation of the speech mechanisms of the two hemispheres of the brain.

The author has collected together a very large amount of material and has produced a volume which cannot be neglected by the physiologist or clinician.

Functional Nervous Disorders. By DONALD E. CORE. Bristol: John Wright and Sons, Ltd. Price 25s. net.

The originality of some of the views expressed in this book give it an interest to the advanced student of psychological medicine.

The classification of the functional disorders is peculiarly the author's own, and is based upon a conception of etiological factors in mental illness, particularly in hysteria, which is likely to be contested by the majority of psychologists at the present time. The functional nervous disorders are divided into regressive and progressive groups, in the former of which he places hysteria, and in the latter the sympathetic nervous disorders. He subdivides the progressive group further into what he terms the Instinct-Distortion Neuroses and the Memory Neuroses. This classification is based mainly on his conception of the term dissociation, which to him means a non-registration of memory of highly emotional incidents. The obsessional neuroses are attributed to relative inattention, dissociation not being operative in the sense in which he uses this term. He suggests that the involvement of the sympathetic nervous system in cases belonging to the progressive group induces in the course of time organic disease.

He is rather scornful of psycho-analysis and concludes that it is logically inapplicable to the treatment of hysteria, though it may be used in the treatment of what he terms the obsessional form of the memory-neurosis. Few psychotherapists of experience will agree with his opinion that the most efficient procedure in analysis is a thorough and searching cross-examination, and not free-association. An interesting chapter is devoted to a study of behaviour in man compared with the lower animals ; the author arrives at the conclusion that although animals have what we term "body-memory," dependent on visceral dispositions specific to emotional tones, they can in no sense be credited with memory as we commonly understand it.

Dr. Coré's views are clearly and carefully reasoned, but a careful study of this book is not likely to diminish the unfortunate confusion of opinion which obtains at the present time with regard to the etiology and treatment of the functional nervous disorders.

Archives of Neurology and Psychiatry. Edited by Sir FREDERICK MOTT. Vol. viii. London County Council. 1922.

This volume contains seventeen articles, all of which except one have been previously published elsewhere, but neurologists and psychiatrists will be grateful to the editor for having collected them together in this accessible form.

A large part of the volume is made up of studies on the pathology of dementia præcox, which are mainly from the pen of the editor. His Morison Lectures on the Psychopathology of Puberty and Adolescence, and his interesting lecture on "Body and Mind: the Origin of Dualism" are also republished here. Dr. Golla's Croonian lectures on the Objective Study of the Neuroses, and Dr. Morowoka's papers on the histology of the choroid plexus in various forms of mental disease, and the effect of exposing the brain to the gamma rays of radium, are also included.

Other interesting contributions are papers on mental defect and criminal conduct by Sir Bryan Donkin, on the neurological aspects of shock by the editor, and on chemical investigations of the cerebrospinal fluid in epilepsy, and on the metabolism in this disease by Mr. Mann.

Anormale Kinder. By L. SCHOLZ. Third edition. Edited by A. GREGOR. Pp. 312. Berlin: S. Karger. 1922.

The study and treatment of abnormal or defective children has been perhaps of recent years more thoroughly developed in Germany than elsewhere in Europe; there attention has been particularly directed to the "social" training of children both at home and in special institutions under the care of adequately equipped teachers and physicians. The system that has been thus elaborated certainly compares very favourably with our more happy-go-lucky methods; it includes the provision of special schools for those who can remain at home, and institutional life for the more defective whose infirmities make it impossible to allow them to mix with the rest of the family.

This book was originally prepared for teachers and officers of institutions for defectives, as well as for the medical students and practitioners; the additions and modifications it has received from its present editor have been developed with the same aim. It is therefore essentially a practical book. The psychology of the child, the various types of mental feebleness and deficiency, and the physical traits associated with them, are first considered. The following chapters deal with nervousness, hysteria, epilepsy and the various psychopathies, but the most striking and valuable portion of the book is that devoted to treatment, education, and training. It is written simply and directly, and can be strongly recommended to all on whom fall the duties of the care and education of the abnormal child.

Psychology.—A Study of Mental Life. By ROBERT S. WOODWORTH. London: Methuen and Co. 1922.

This book is intended for students beginning the study of psychology, and its aim is to represent to them in simple and reasoned fashion the present state of this very active science. In this aim it succeeds exceedingly well, and it should prove a useful and stimulating textbook on the subject. It has a distinctly physiological setting, which adds to its value as a textbook.

Defining psychology as the science of behaviour, it studies first the simplest forms of behaviour as illustrated in reflexes and elementary forms of stimulus response, and then passes to the discussion of sensations, perceptions and thoughts as the reactions of higher nervous levels to stimuli of different kinds. The "stimulus response" theory is then enlarged to include motives, interests and purposes as predisposing tendencies to the production of the different reactions and responses that constitute behaviour. From this there follows naturally a division of behaviour into native and acquired reactions, and a consideration of these two classes in detail. Several chapters are devoted to the instincts and their accompanying emotions, to feeling tone and the various sensations, to attention and intelligence, until, finally, we come to the discussion of learning and habit formation, of memorizing and the laws that govern the association of mental processes of perception, reasoning, imagination and the will. Last of all there is a chapter on Personality.

The "unconscious" is dealt with adequately, and while very considerable credit is given to the originality and value of Freud's views there is some very sane and unimpassioned adverse criticism, which is not the least valuable part of the book from the beginner's point of view.

Medizinische Psychologie. By Dr. ERNST KRETSCHMER. Leipzig: Georg Thieme. 1922.

Even to students and practitioners who have chosen the mental illnesses as their special department this little handbook will be found of great interest and value. Unlike the majority of textbooks on this subject it does not deal with the disorders of the mind in a purely descriptive fashion, but treats them on strictly scientific lines as results of disturbances of normal psychological processes.

Acknowledging the debt that psychiatry owes to normal psychology he passes on to a consideration of mental development, paying particular attention to the part played by the emotions, and discusses the theory of ambivalence and the part it takes in complicating the affective life of the individual. The precise position of dream experience is discussed in its relation to the conscious life of the subject, and to that part of it which lies outside the immediate sphere of awareness. From this the author naturally passes on to a consideration of the state of hypnosis, and thence to hysteria and schizophrenia. The chapter on the Instincts is particularly good in that the normal and the abnormal are treated together, bringing home very forcibly the fact that in al divergences from normal behaviour the underlying processes are psychologically unchanged, but inadequate to the immediate reality at the time.

The last chapter discusses fully all the present-day technical methods of investigating mental illnesses from the psychological point of view, and the necessary therapeutic measures. He appears to be sympathetically disposed towards the Freudian technique, but does not rule out other methods.

The Poetic Mind. By FREDERICK C. PRESCOTT. New York: Macmillan and Co. 1922.

The author has applied the results of recent psychological investigations to the subject of poetic inspiration, and has produced a closely reasoned and well informed book. His outlook is primarily literary rather than psychological; psychological concepts are used to elucidate the nature of the poetic impulse without any desire to make a contribution to pure psychology. At the outset the author prepares us for his opinion that the treatment of the poet's mind must result in general conclusions, and not in the scientific formulæ of a fixed science of æsthetics. The poet's fancy springs from the vicissitudes of personal experience, expressed in dream-like form, shaped by imagination and contorted by repression, springing forth to "cleanse the bosom of that perilous stuff which weighs upon the heart."

It is certainly one of the books on psychology applied to art that repays reading; it is well written as befits a literary theme, tentative, sober and suggestive.

Ueber die Bedeutung und Entstehung der Stereotypien. By JAKOB KLÄSI. Pp. 109. Berlin: S. Karger. 1922. M. 30.

Stereotypy, as defined by the author, is the autonomous manifestations of motor, speech or psychical functions reiterated over long periods in exactly the same form, and neither associated with any emotion, nor adapted to any objectively purposive end. He distinguishes two main types; those of the one group are either determined by hallucinations and can be consequently regarded as forms of defence reaction, or they may be interpreted as ceremonies or incantations for the reinforcing or symbolizing of a rite resulting from a delusion or hallucination. Stereotypies of the other group are relics of a former occupation or habit and were consequently originally purposive; these are distinguished by the fact that they can be easily modified and altered.

This monograph is a valuable study in a difficult and rather neglected region of psychopathology.

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EDITOR.

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BRAIN.

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RÉFLEXES DE DÉFENSE.[1]

PAR J. BABINSKI.

MESSIEURS,—J'ai entendu raconter l'anecdote suivante : le grand seigneur espagnol auquel Cervantes a dédié son livre " Don Quichotte," voyageant en France arrive à une heure tardive dans une localité où il se propose de passer la nuit. Il sonne à une auberge dont le patron, avant d'ouvrir la porte, demande à qui il a affaire. Le noble gentilhomme décline ses noms : Duque de Bejar, Marques de Gibraleon, Conde de Bañalcazar y Bañares, Visconde de la Puebla de Alcocer, Señor de las Villas de Capilla, Curiel y Burguillos. L'aubergiste, qui ignorait qu'un espagnol pouvait avoir six ou huit noms différents, réplique : Messieurs, vous êtes beaucoup trop nombreux, je ne puis vous loger ; il laisse le seigneur dans la rue et se prive ainsi d'un hôte qui lui aurait valu un beau bénéfice. Une mésaventure un peu analogue est arrivée à un étudiant en médecine désireux d'apprendre la sémiologie des maladies du système nerveux. Parcourant la table des matières d'un livre qu'on lui avait recommandé, il trouve en particulier, pour ce qui concerne l'examen des membres inférieurs, l'indication des signes suivants : réflexes de défense, réflexe antagoniste de Schaefer, Unterschenkelphaenomen d'Oppenheim, réflexe fléchisseur dorso-plantaire de Bechterew, triple retrait du membre inférieur, phénomène des raccourcisseurs, réflexes d'automatisme médullaire, massreflex. Ne sachant pas que toutes ces dénominations se rapportaient, au moins en très grande partie, à un seul et même phénomène, et se jugeant incapable de loger dans son esprit tant de données qu'il croyait différentes, il renonça à cette étude et se priva ainsi d'une notion facile à acquérir et qui lui aurait été très utile.

Je ne veux pas soutenir que le sujet dont je me propose de vous entretenir soit en tous points définitivement fixé et ne comporte plus de discussion ; vous verrez dans la suite qu'il n'en est pas ainsi ; mais je crois pouvoir dire que la question est fort simple en ce qui regarde la clinique, les moyens qu'il faut employer pour mettre en évidence les réflexes dont nous allons nous occuper et certaines conséquences que l'on peut en déduire pour le diagnostic.

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[1] A Lecture delivered at the Royal Society of Medicine, London, with presentation of cases and cinematograph films.

Me plaçant d'abord sur le terrain de l'observation et écartant les interprétations pathogéniques, je vais décrire les phénomènes que j'ai en vue. Il s'agit de réactions motrices consécutives à des excitations cutanées ou à des excitations profondes. Pour commencer, j'envisagerai uniquement les réactions observées aux membres inférieurs du côté excité, faisant abstraction des orteils (c'est là une dissociation artificielle il est vrai, mais vous verrez ultérieurement pourquoi je la fais) et me bornant à observer les mouvements exécutés par le pied, la jambe et la cuisse. Voici en quoi consistent ces réactions : sous l'influence d'excitations du membre inférieur telles que le frottement de la plante du pied avec une épingle, le pincement de la peau de la région dorsale du pied ou de la jambe, notamment à sa partie inférieure, il se produit, outre une contraction du fascia lata, une flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin ; l'attitude en flexion se maintient généralement un laps de temps appréciable et le membre inférieur ne reprend qu'avec une certaine lenteur son attitude primitive ; dans certains cas, la contraction musculaire dure dix, quinze secondes, davantage même, surtout si l'excitation qui a provoqué le mouvement est continue, et il est possible quelquefois de déterminer ainsi une sorte de contracture transitoire.

Ce mode de réaction (triple flexion) susceptible d'être obtenue par des excitations portant sur diverses parties du membre inférieur est un des plus communs et l'on a couramment l'occasion de l'observer en clinique. On le constate ordinairement chez des malades présentant des troubles notables de la motilité volontaire, et c'est là qu'il acquiert le maximum d'intensité, mais il peut être très net chez des sujets encore assez valides.

L'électrisation avec des courants voltaïques ou avec des courants faradiques, l'application d'un corps chaud ou d'un corps froid, la pression exercée sur les parties profondes, les tractions constituent aussi de bons procédés d'excitation. Bechterew, puis Pierre Marie et Foix, ont recommandé une manœuvre indiquée déjà par Charcot et qui consiste à fléchir fortement les orteils sur la plante, en même temps qu'on abaisse l'extrémité antérieure du pied.

La zone réflexogène est plus ou moins étendue suivant les malades. Souvent, elle occupe seulement le pied et la jambe et s'arrête approximativement au genou, mais parfois elle s'étend même à la cuisse et à une partie plus ou moins vaste du tronc ; nous reviendrons ultérieurement sur ce point. Dans certains cas, tandis que l'excitation du pied et de la jambe donne lieu au movement habituel, c'est à dire à la triple flexion, une irritation portant sur la cuisse est suivie d'une extension des trois segments. Voici une autre modalité de la réaction dont je m'occupe : le pincement de la peau de la partie inférieure de la jambe est suivi d'une flexion du pied et d'une extension de la jambe sur la cuisse ; j'ai particulièrement observé cette modalité chez des malades plus ou moins contracturés, dont les jambes, qui d'habitude se maintenaient en extension, avaient été préalablement placées par moi en demi-flexion. Il m'est arrivé aussi de voir ceci : l'excitation, provoquant toujours une flexion du pied, accentuait un peu, pour commencer, l'attitude de la jambe en flexion, laquelle était immédiatement suivie d'un fort mouvement en sens inverse qui ramenait la jambe en extension. Parfois, quel que soit le sens du mouvement, flexion ou extension, on constate des contractions dans les muscles de groupes opposés, et l'on peut concevoir que le sens du mouvement soit conditionné en partie par la position où se trouvent au moment de l'excitation les segments du membre les uns par rapport aux autres.

Il y a de grandes différences en ce qui concerne l'intensité des réflexes, l'amplitude des mouvements. Tantôt, le moindre attouchement de la peau d'un membre suffira à déclencher une flexion très prononcée de tous ses segments et amènera une série de mouvements alternatifs de flexion et d'extension ; tantôt, au contraire, le pincement très vif de la peau ne déterminera qu'avec peine une simple flexion du pied. Entre ces types extrêmes se placent tous les intermédiaires. En outre, il est à remarquer que si, pour chaque malade, il existe, au cours d'un examen, une certaine proportionalité entre l'intensité de l'excitation et celle de la réaction, le rapport entre ces deux éléments peut varier notablement lorsque l'on considère les résultats de deux examens pratiqués à quelques jours ou même à quelques heures d'intervalle.

La description qui précède se rapporte à des observations faites sur des sujets atteints d'affections organiques intéressant la voie pyramidale.

Mais, avant d'aller plus loin, je dois discuter les questions suivantes : les réactions signalées sont-elles toutes pathologiques ; quelques-unes d'entre elles peuvent-elles au contraire être obtenues à l'état physiologique ; y a-t-il des caractères permettant d'affirmer la nature pathologique de ces réactions ou de quelques-unes d'entre elles ?

Pour résoudre le problème, il est indispensable d'avoir examiné un grand nombre d'individus normaux et de savoir comment chez eux les membres inférieurs se comportent vis-à-vis d'excitations diverses. Or, voici ce qui paraît bien établi. Une excitation de la plante du pied telle que le frottement avec une épingle est souvent suivie, élimination faite du mouvement des orteils sur lequel je reviendrai ultérieurement, d'une contraction du fascia lata que Brissaud a très bien décrite et d'une flexion du pied, de la jambe et de la cuisse. Ce sont là les mêmes mouvements que ceux qu'on observe à l'état pathologique. Mais chez le sujet normal la contraction est rapide, de courte durée, tandis que chez les malades dont il est question l'attitude en flexion obtenue par l'excitation plantaire se maintient généralement quelque temps et ne reprend que lentement sa position primitive, ainsi que je l'ai dit précédemment ; en outre chez ces derniers, l'amplitude du mouvement est bien plus marquée d'habitude. Ces différences sont souvent suffisantes pour établir une ligne de démarcation nette entre l'état physiologique et l'état pathologique. Toutefois, en se fondant uniquement sur ce qui vient d'être dit, des médecins encore peu expérimentés en clinique neurologique et n'ayant pas la vision précise de la forme des mouvements réflexes pathologiques seraient exposés à des erreurs ; ajoutons à cela que ces mouvements n'ont pas toujours la lenteur ci-dessus décrite.

Un autre caractère plus important et conduisant à distinguer l'état physiologique de l'état pathologique est le suivant : chez l'homme normal, l'excitation d'une région quelconque du membre, *hors de la plante du pied*, si elle peut provoquer un mouvement de flexion de la cuisse et de la jambe, ne donne jamais lieu à la flexion du pied. Je crois utile d'appuyer sur ce point. Sans doute, le retrait de la cuisse et celui de la jambe qu'on peut observer alors semblent volontaires et diffèrent d'habitude des réactions réflexes par les caractères du mouvement, ainsi que par ce fait que la contraction spéciale du tenseur du fascia lata signalée plus haut fait défaut ; mais, je le répète, sans autres moyens distinctifs, la confusion entre l'état physiologique et l'état pathologique pourrait être malaisée à éviter. Au contraire, l'absence pour ainsi dire constante de la flexion du pied chez le sujet normal (exception faite pour un cas de simulation qu'on pourrait d'ailleurs dépister) rend simple la solution du problème. *La flexion du pied obtenue par l'excitation d'une autre région que la plante du pied permet d'affirmer qu'on a affaire à un état morbide.*

Ce signe à lui seul me paraît donc décisif ; c'est le criterium de l'état pathologique. Il va sans dire que la conviction qu'il entraîne ne peut que se fortifier lorsque ce caractère s'associe au précédent, à la lenteur de la contraction et surtout de la décontraction. Au risque de décourager l'étudiant dont je vous parlais au début de cette Conférence, je propose une expression nouvelle : "*signe de la flexion réflexe du pied*" pour désigner les réflexes pathologiques que nous étudions. Le moyen le plus simple pour constater ce phénomène est de pincer la peau du dos du pied ou de la partie inférieure de la jambe. J'insiste auprès de ceux de mes auditeurs qui sont des débutants sur l'intérêt qu'il y a à connaître ce signe, lequel a le double mérite d'être d'une exploration très facile et d'avoir une grande valeur clinique puisqu'il décèle l'existence d'une perturbation de la voie pyramidale, que celle-ci siège dans l'encéphale ou dans la moelle. S'ils retiennent seulement cette donnée, j'aurai la satisfaction de croire qu'ils n'ont pas perdu l'heure qu'ils ont bien voulu me consacrer.

* * * * * *

Le retrait du membre inférieur, et notamment la flexion du pied, a manifestement des rapports assez étroits avec le signe des orteils, puisque ces deux phénomènes paraissent bien caractéristiques d'une perturbation de la voie pyramidale ; ces deux réactions motrices se produisent généralement dans les mêmes conditions et suivant un mode semblable ; je viens de dire que dans la triple flexion la contraction et surtout la décontraction sont lentes ; or, dans mon travail sur le phénomène des orteils, en 1898, je faisais déjà remarquer que le plus souvent l'extension des orteils (réaction pathologique) est exécutée avec plus de lenteur que la flexion des orteils (réaction normale). Je suis très porté à admettre—j'y reviendrai plus loin—que la pathogénie du signe des orteils ressemble à celle de la triple flexion. Mais envisageant la question du point de vue clinique et, comme je l'ai dit dans mon travail sur les réflexes de défense publié en 1914, " mettant absolument de côté tout ce qui concerne l'interprétation physiopathologique de ces phénomènes," j'ai soutenu que les liens entre les réflexes dits de défense et le phénomène des orteils ne sont pas indissolubles, que par conséquent il y avait lieu de ne pas les fusionner complètement.

MM. Marie et Foix, tout en admettant qu'ils peuvent être dissociés et tout en reconnaissant que je n'ai pas prétendu qu'il y eût différence absolue de nature entre le signe des orteils et les réflexes cutanés de défense, déclarent être d'un avis contraire au mien. " Pour nous, au contraire," écrivent nos collègues, " le signe de Babinski appartient à l'ensemble des mouvements automatiques complexes dont le mécanisme est un mécanisme de marche."

M. Walshe, sans être d'accord avec les auteurs précédents sur le mécanisme de ces réactions motrices, ne veut établir aucune distinction entre ces deux phénomènes et il écrit que tandis que je regarde la triple flexion comme de nature défensive, je considère l' " extensor response " comme un réflexe distinct et séparé, une chose à part pour laquelle je n'offre pas d'explication et qui resterait pour moi un signe mystique et inexplicable d'affection du faisceau pyramidal. Je répondrai à cela que, si je n'ai pas cherché à expliquer le phénomène des orteils quand je l'ai décrit, je n'ai jamais dit qu'il fût inexplicable, et je ne vois pas bien ce qu'il y a de mystique à se cantonner dans le domaine de l'observation clinique : j'aurais plutôt mérité le reproche d'être " terre à terre."

Il est incontestable, je le répète, que l'extension réflexe des orteils et la flexion réflexe du pied sont, dans la majorité des cas, associées et je serais sans doute le dernier à le nier, ayant été le premier à signaler en 1900, à propos du travail de Schaefer sur le réflexe antagoniste du pied, dont je vous entretiendrai dans un instant, que, dans l'hémiplégie organique, le pincement de la peau en diverses parties du pied et de la jambe peut provoquer à la fois ces deux réactions. Mais, encore une fois, l'une peut se produire sans l'autre. On peut observer non seulement le phénomène des orteils en l'absence du signe de la flexion réflexe du pied mais aussi la disposition inverse.

J'ai cité autrefois, à l'appui de mon opinion, une Observation anatomo-clinique relatée par Dejerine, Lévi-Valensi et Long [14, 15] : il s'agissait d'un cas de paraplégie par section complète de la moelle où il existait, en même temps que des réflexes de défense très nets, une flexion plantaire des orteils des plus franches ; il est à remarquer qu'il n'y avait pas trace de réaction de dégénérescence dans les muscles de la jambe. M. Walshe récuse cette Observation à cause du passage suivant qu'on y trouve : " Les pieds sont en varus équin et les orteils en flexion. Cette déformation est aujourd'hui fixée par des rétractions fibro-musculaires." La critique de M. Walshe n'est pas sans valeur. Mais il y a tout lieu de penser que ces rétractions n'étaient pas assez marquées, au moins pendant un certain laps de temps, pour entraver l'exploration des réflexes, car M. Dejerine donne à cet égard des renseignements tellement circonstanciés qu'un doute ne peut guère subsister. Il écrit en effet : " J'arrive maintenant à une question encore plus importante peut-être que les précédentes, à savoir l'état du *réflexe cutané plantaire*. Pendant les six mois que passa ce malade dans mon service, le réflexe cutané de la plante du pied se faisait des deux côtés en flexion plantaire, c'est à dire comme à l'état physiologique."

Je rappelle aussi l'observation publiée par Pastine [27] se rapportant a un sujet atteint de paraplégie motrice absolue avec troubles très accentués de la sensibilité superficielle et profonde des membres inférieurs. J'extrais de ce travail le passage suivant : " Le fait intéressant pour la question qui nous occupe me semble être celui-ci : la possibilité presque constante d'obtenir, par une excitation plantaire un peu forte ou répétée, ou encore mieux par un pincement énergique de la peau du dos des pieds, le mouvement réflexe de flexion du pied, de la jambe et de la cuisse associé à la flexion nette de tous les orteils, et par une excitation minimale du bord plantaire externe, le signe de Babinski nettement positif et isolé. Dans ce cas, c'est la flexion du gros orteil qui fait partie du mouvement général de retrait, et pourtant l'extension pathologique du même orteil existe dans toute sa pureté."

Du reste, déjà dans un travail publié par moi en mars 1899 [2], basé en particulier sur une observation qui est un type de paraplégie en flexion, avec mouvements spasmodiques intermittents accentuant la flexion des cuisses et des jambes, il est dit expressément que le réflexe cutané plantaire est normal.

Des expériences de M. Ozorio de Almeida, confirmées par moi, ont montré que chez des sujets présentant le signe des orteils, une compression du membre inférieur avec une bande élastique peut amener transitoirement la réapparition du mouvement réflexe de flexion des orteils ; or, le pied peut continuer alors à exécuter un mouvement réflexe en flexion à la suite de l'excitation de sa région dorsale.

MM. Marie et Foix, dans un article sur "les réflexes d'automatisme médullaire [22]," écrivent à ce sujet : "Nous avons, sur la plupart de ces points, pu reproduire les expériences de Babinski, mais l'interprétation que nous inclinons à donner nous apparaît comme très différente de la sienne" . . . . "Il est aisé de se convaincre par l'observation attentive que l'application de la bande d'Esmarch agit en supprimant momentanément l'excitabilité réflexe des muscles ischémiés . . . ." Les muscles extenseurs, par suite des dispositions anatomiques, subiraient une ischémie plus intense que les fléchisseurs.

L'interprétation donnée par mes collègues me semble discutable. Elle ne permet guère de comprendre ce fait noté chez certains sujets et que je rappelle : avant la compression, réflexe plantaire toujours en extension quelle que soit la région de la plante que l'on excite ; après la compression, réflexe en extension ou en flexion suivant qu'on excite le bord externe ou le bord interne de la plante.

De plus, en variant la durée de la compression, j'ai fait plusieurs fois les constatations suivantes : après avoir enlevé la bande à un moment où le réflexe se faisait encore en extension, j'ai vu cependant, au bout de quelques instants, au retour de l'irrigation sanguine, le réflexe en flexion remplacer pour quelque temps le mouvement réflexe précédent. Il m'est arrivé alors d'observer, après avoir pincé la peau de la jambe ou du dos du pied, la flexion des orteils associée à une forte flexion du pied.

Ces faits ne sont guère en concordance avec l'interprétation proposée par MM. Marie et Foix. D'ailleurs, celle-ci serait-elle juste, elle n'infirmerait pas ma thèse, car me plaçant simplement sur le terrain de l'observation, et sans contester aucunement les relations qui unissent la flexion réflexe du pied avec l'extension des orteils, les connaissant même depuis plus de vingt ans, comme je viens de le dire, j'ai voulu établir qu'il pouvait y avoir dissociation de ces deux phénomènes. Les cas où cette dissociation existe, sans être très communs, ne sont pas tout à fait exceptionnels; j'en ai observé déja un assez grand nombre et vous aurez l'occasion de la constater vous-mêmes sur l'un des films que je ferai passer devant vos yeux. Il s'agit d'un malade atteint de paraplégie incomplète liée vraisemblablement à une plaque de sclérose: d'un côté on observe la trépidation épileptoïde du pied et le triple retrait associé à l'extension du gros orteil; de l'autre côté la trépidation épileptoïde et le triple retrait existent nettement, mais ce dernier phénomène coïncide avec un réflexe plantaire en flexion bien qu'il n'existe pas de réaction de dégénérescence dans les muscles de la jambe.

Avant de terminer ce chapitre, je ferai remarquer que Marie et Foix, malgré leur désaccord apparent avec moi, semblent avoir dans le fond une opinion analogue à la mienne, puisque dans leur premier article sur le retrait réflexe du membre inférieur [21] ils écrivent ceci: "Il (le retrait réflexe) est extrêmement fréquent dans l'hémiplégie constituée. Il est en général associé au signe de Babinski, mais ne lui est pas superposable. On l'observe en effet en dehors de ce signe, particulièrement chez certains pseudo-bulbaires, ou dans certains cas d'hémiplégie ancienne"; et, dans un deuxième travail sur les réflexes d'automatisme médullaire [22], ils écrivent encore: "L'on peut cependant voir, dans les cas où, par suite du combat entre le réflexe normal en flexion et le réflexe pathologique en extension, le mouvement des orteils est nul ou même en flexion, le signe des raccourcisseurs établir une lésion que la recherche du signe de Babinski n'avait pu dépister."

N'est-ce pas absolument conforme à ce que j'ai soutenu?

Il me semble intéressant, à l'appui de ma thèse, de noter que M. Van Woerkom, dans un travail "Sur la signification physiologique des réflexes cutanés des membres inférieurs" [33], écrit ceci: "Pourtant, le lien qui relie le signe de Babinski au 'flexion réflexe' n'est pas indissoluble."

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Contrairement à l'usage suivant lequel l'exposé d'une question est généralement précédé de l'indication des noms de ceux qui s'en sont principalement occupés, j'ai cherché d'abord à faire une description des faits cliniques suffisante pour bien délimiter mon sujet. Je crois le moment venu de faire un historique, surtout étant donné que j'ai déjà été entraîné à signaler quelques controverses entre neurologistes.

Les phénomènes que nous étudions paraissent avoir été mentionnés pour la première fois en 1784 par Prochaska. L'expérience faite par cet auteur a été maintes fois reproduite depuis ; Schiff, Vulpian, Brown-Séquard, pour ne citer que quelques-uns des physiologistes qui se sont occupés des réflexes de défense, ont vu comme Prochaska qu'une grenouille ou un mammifère dont on sectionne la moelle dorsale retire brusquement la patte en fléchissant les divers segments de ce membre les uns sur les autres quand on en pique l'extrémité.

Ce mouvement reproduit assez exactement celui qu'effectue, sous la même excitation, une grenouille dont la moelle est intacte et qui cherche à se dérober à l'injure extérieure, à se défendre. Le phénomène fut pour cela qualifié de " mouvement réflexe de défense," et l'usage a consacré cette dénomination.

Les physiologistes seuls s'occupèrent d'abord de ces mouvements particuliers. Vulpian, Brown-Séquard signalent il est vrai leur existence dans les tumeurs de la moelle et dans quelques autres affections de cette partie du névraxe, mais ils n'en indiquent pas la valeur séiniologique précise.

L'attention qu'on leur avait prêtée fut même bientôt très réduite lorsqu'on acquit la connaissance des réflexes tendineux et qu'on s'attacha à leur étude. La brièveté des mentions qu'on trouve au sujet des réflexes de défense dans les meilleurs traités classiques de neurologie fait foi, d'ailleurs, de ce réel discrédit.

C'est depuis vingt-cinq ans environ, et à la suite de ma communication sur le réflexe cutané plantaire et le phénomène des orteils, que l'attention a été de nouveau dirigée sur les réflexes de défense, bien qu'on se soit servi parfois d'autres termes pour désigner les faits qui s'y rapportaient.

Schaefer, dans un travail publié en novembre 1899 [31], décrit un phénomène réflexe dont voici les caractères : lorsqu'on presse énergiquement, entre le pouce et l'index, le tendon d'Achille dans son tiers moyen ou son tiers supérieur, on provoque chez l'individu sain une sensation de douleur légère et en même temps une très faible extension du pied et parfois aussi une flexion des orteils. Or, dans certains cas pathologiques, chez des malades atteints d'hémiplégie cérébrale organique, la même manœuvre donne lieu à une sensation de douleur plus intense et, en outre, à une flexion du pied ainsi qu'à une extension des orteils du côté paralysé. Ce réflexe pathologique se distinguerait des autres réflexes tendineux parceque la réaction, au lieu de s'opérer dans le muscle dont le tendon est excité, se manifesterait dans les antagonistes, d'où la dénomination de *réflexe antagoniste* que Schaefer propose de donner à ce phénomène.

Ainsi que je l'ai dit dans une communication à la Société de Neurologie en janvier 1900, il est aisé de vérifier les faits décrits par Schaefer qui sont absolument exacts, mais ses déductions comportent des critiques : d'une part, l'extension des orteils qu'il indique n'est autre chose que le phénomène des orteils découvert antérieurement ; d'autre part, rien n'autorise à admettre que la réaction obtenue dans les expériences de Schaefer constitue un réflexe tendineux antagoniste. J'ai montré, en effet, que chez les hémiplégiques qui présentent ces réactions, extension des orteils et flexion du pied, celles-ci sont généralement obtenues par le pincement de la peau seule dans le voisinage du tendon ou encore en d'autres parties du membre inférieur. Comme on le voit, ces observations ont conduit à cette notion nouvelle, dont j'ai fait ressortir précédemment l'intérêt, qu'une excitation du membre inférieur, hors de la zone plantaire, incapable de produire une flexion réflexe du pied à l'état normal, peut en déterminer une dans l'hémiplégie organique, affection dans laquelle la voie pyramidale est intéressée.

Les réactions décrites ultérieurement par Oppenheim sous la dénomination d' " Unterschenkelphaenomen " dans les affections pyramidales sont identiques aux précédentes. Voici en quoi elles consistent : tandis que l'excitation des téguments de la partie interne de la jambe provoquée par le frottement ne détermine à l'état normal aucun réflexe, ou seulement une flexion des quatre petits orteils, cette excitation, dans les cas où il y a une lésion de la voie pyramidale, produit une contraction des muscles extenseur propre du gros orteil, jambier antérieur, extenseur commun des orteils et parfois des muscles péroniers.

Van Gehuchten [32], en août 1900, dans une étude " sur les réflexes cutanés et les réflexes tendineux," s'occupe particulièrement des réflexes de défense dans les lésions atteignant le système pyramidal ; il se sert de ces termes : " mouvement de retrait brusque de tout le membre : flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin, avec mouvements d'adduction de la cuisse."

Je reviens sur ce sujet dans un travail publié en 1904 à la Société de Neurologie et intitulé : " Sur la transformation du régime des réflexes cutanés dans les affections du système pyramidal."

Bechterew [11] en 1906 a publié une note sur les mouvements réflexes produits par la manœuvre qui consiste à flechir le pied et les orteils.

En mai 1910, nous cherchons, Jarkowski et moi [7], à utiliser les réflexes de défense pour déterminer le niveau inférieur d'une lésion spinale.

En juillet 1910, Pierre Marie et Foix publient leur premier travail sur ce sujet [21]. Il est intitulé : " Sur le retrait du membre inférieur provoqué par la flexion forcée des orteils."

En 1910 Claude [13] traite de l'hyperkinésie réflexe qu'on peut observer au membre supérieur.

En janvier 1911 [3], je décris "la paraplégie spasmodique avec contracture en flexion et contractions musculaires involontaires" et je fais ressortir les liens qui l'unissent aux réflexes de défense. En mai 1912, je reviens sur ce sujet [4].

Nouveau travail de Marie et Foix en mai 1912 [22], intitulé : "Les réflexes d'automatisme médullaire et le phénomène des raccourcisseurs. Leur valeur sémiologique. Leur signification physiologique."

En 1912, mémoire de van Woerkom [33] : "Sur la signification physiologique des réflexes cutanés des membres inférieurs."

En 1914-1915 [6], je publie une étude sur les réflexes de défense, et quelques semaines plus tard Pierre Marie et Foix [23] font paraître à leur tour un mémoire sur "les réflexes d'automatisme médullaire dits de défense."

Dans un travail intitulé : "Quelques remarques sur les réflexes de défense dits d'automatisme médullaire" [18], Jarkowski discute la pathogénie de ces phénomènes.

Voici maintenant l'indication de plusieurs travaux sur le sujet qui nous occupe qui sont l'œuvre de neurologistes anglais :

F. M. R. Walshe : "The Physiological Significance of the Reflex Phenomena in Spastic Paralysis of the Lower Limbs" [34], et "On the Genesis and Physiological Significance of Spasticity and other Disorders of Motor Innervation" [35].

Henry Head and George Riddoch : "The Automatic Bladder, Excessive Sweating and some other Reflex Conditions in Gross Injuries of the Spinal Cord" [17].

George Riddoch : "The Reflex Functions of the Completely Divided Spinal Cord in Man" [28], et "The Clinical Picture of Complete Transverse Division of the Spinal Cord" [29].

George Riddoch and Farquhar Buzzard : "Reflex Movements and Postural Reactions in Quadriplegia and Hemiplegia, with especial reference to those of the Upper Limb" [30].

Je fais une place à part au grand physiologiste Sherrington dont les découvertes ont orienté les recherches des neurologistes anglais et les ont inspirés dans leurs interprétations des faits cliniques observés. Le nom de Philipson, collaborateur de Sherrington, mérite aussi d'être particulièrement retenu.

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Après ce court historique, reprenons le fil de nos idées. J'ai dit que si le lien entre les réflexes de défense pathologiques, notamment la flexion réflexe du pied et le signe des orteils, n'est pas indissoluble, il est pourtant assez étroit.

Et quelles sont les relations entre ces diverses réactions et la surréflectivité tendineuse qui elle aussi constitue une signe de perturbation de la voie pyramidale ? On peut dire, a priori, que ces deux ordres de phénomènes doivent être souvent associés, mais c'est une liaison beaucoup moindre que la précédente. Dans le tabes dorsal spasmodique avec surréflectivité tendineuse extrêmement forte, la flexion réflexe du pied est généralement faible ou même fait défaut, ce qui, à la vérité, pourrait tenir à la contracture en extension qui entrave la manifestation des réflexes de défense. Dans l'hémiplégie organique avec exagération notable des réflexes tendineux et trépidation épileptoïde, la flexion réflexe du pied peut aussi manquer de même qu'il y a parfois absence du signe des orteils.

Mais ce qui est plus frappant c'est la disposition inverse : affaiblissement ou abolition des réflexes tendineux avec exagération notable des réflexes de défense. C'est ce qu'on observe d'habitude dans la maladie de Friedreich ; c'est ce qu'on peut voir dans le tabes associé à une lésion pyramidale. J'ai insisté déjà en 1898, dans un travail relatif au phénomène des orteils [1], sur la coexistence de ce signe avec la subréflectivité ou l'irréflectivité tendineuse. "J'ai constaté, disais-je, ce phénomène dans plusieurs cas d'hémiplégie récente flasque, où les réflexes tendineux étaient normaux, affaiblis ou même abolis du côté paralysé."

On observe très couramment des malades atteints de paraplégie crurale plus ou moins marquée avec réflexes tendineux normaux, sans trace de trépidation épileptoïde du pied et avec réflexes de défense très caractérisés. Je suis convaincu, certain même, qu'autrefois beaucoup de malades de ce genre ont été considérés comme atteints de paraplégie hystérique. Ces erreurs sont devenues bien plus rares depuis que la connaissance des signes en question s'est répandue parmi les praticiens.

Dans la paraplégie en flexion, sur laquelle je reviendrai plus loin et dont le trait le plus essentiel est l'exagération des réflexes de défense, les réflexes tendineux peuvent aussi être exagérés, mais il n'en est pas toujours ainsi : ils sont parfois d'une intensité moyenne, ils peuvent être faibles et semblent même abolis dans certains cas Je sais bien que l'exploration des réflexes tendineux est rendue quelquefois difficile par les rétractions fibro-tendineuses, par l'intensité et la fréquence des spasmes qui se produisent ; mais en renouvelant les explorations à plusieurs reprises, en saisissant, pour les pratiquer, les moments où le spasme cesse, il est ordinairement possible de se rendre compte de l'état de la réflectivité tendineuse. Si j'ai bien compris ce qu'a écrit M. Walshe à ce sujet, il est d'avis que dans la paraplégie en flexion, si les réflexes tendineux des extenseurs peuvent être abolis, ceux des fléchisseurs sont toujours exagérés. Je ne puis souscrire à cette opinion, m'étant assuré dans quelques cas de paraplégie en flexion que les réflexes tendineux des fléchisseurs de la jambe sur la cuisse n'étaient pas du tout au-dessus de la normale et paraissaient même plutôt faibles.

Dans la paraplégie en flexion, l'affaiblissement des réflexes tendineux peut survenir après une période plus ou moins longue pendant laquelle il y a eu surréflectivité tendineuse. Mais il y a des cas où, dès le début, les réflexes tendineux sont amoindris. J'ai rapporté une Observation de ce genre ; voici un passage du travail où ce fait est relaté [4] : " Ce qui est capital c'est que, chez cette malade, où l'existence d'une affection organique de la moelle intéressant les faisceaux pyramidaux est incontestable, on observe une contracture associée à une abolition à peu près complète des réflexes tendineux et à des réflexes de défense extrêmement forts. Ce fait constitue un nouveau document relatif à l'histoire de la *paraplégie spasmodique organique avec contracture en flexion et contractions musculaires involontaires*, et il mérite pour plusieurs motifs d'attirer l'attention.

" Tandis que, chez les sujets où la contracture en flexion est permanente et a acquis une grande intensité, la faiblesse ou l'abolition des réflexes tendineux est difficile à apprécier et ne peut être affirmée qu' après des examens plusieurs fois renouvelés ; dans le cas particulier, la contracture en flexion étant intermittente, on est à même, pendant les phases de détente qui sont très fréquentes, de se rendre un compte exact des réflexes tendineux ; on s'assure aisément que le réflexe rotulien droit et les réflexes achilléens sont abolis. J'ajoute que l'affaiblissement des réflexes tendineux a été noté, dans ce cas, dès le début de l'affection et n'a pas été précédé de l'exagération de ces réflexes, ainsi que cela se voit assez souvent dans cette forme de paraplégie."

* * * *

L'exagération des réflexes de défense conduit-elle seulement au diagnostic de perturbation de la voie pyramidale ? N'est-elle pas en mesure de fournir d'autres renseignements ayant une portée pratique, notamment dans les cas de compression de la moelle ? C'est une question que nous avons cherché à résoudre, Jarkowski et moi. Mais il est de mon devoir de signaler un passage relatif à ce sujet que j'extrais de l'ouvrage de Duchenne de Boulogne " De l'électrisation localisée " et qui nous avait échappé autrefois : " Le point où le chatouillement de la peau cesse de provoquer des contractions réflexes indique le niveau où existe la compression de la moelle." Il est à noter que ce moyen de localisation n'avait jamais été utilisé jusqu'à nous par aucun des neurologistes qui s'étaient occupés de repérer les tumeurs comprimant la moelle en vue de l'intervention chirurgicale. Voici, en résumé, ce que nous avons cru pouvoir déduire de nos investigations : Dans tout le territoire cutané en rapport avec la portion de la moelle sous-jacente à la partie inférieure de la lésion et dans ce territoire seulement, du moins quand la paraplégie est très marquée, une excitation peut provoquer des réflexes de défense. On possède ainsi un moyen de déterminer la limite inférieure de la compression. Ce n'est pas là une vue théorique. Cette donnée est établie déjà sur un certain nombre d'observations où le diagnostic a été vérifié pendant l'opération.

On a aussi publié, il est vrai, quelques faits qui tendent à infirmer cette notion, mais la contradiction n'est peut-être qu'apparente et j'ai cherché à l'expliquer dans mon travail de 1914, dont j'extrais le passage suivant :

" Cela tient, je pense, aux difficultés nombreuses que l'on rencontre quand on s'efforce de délimiter le territoire des réflexes de défense. On est exposé à des erreurs d'observation et d'interprétation sur lesquelles je crois devoir insister.

" C'est ainsi que chez des malades ayant conservé en partie leur motilité volitionnelle, un mouvement volontaire pourrait faire prendre le change et être considéré à tort pour un réflexe de défense. Chez d'autres malades, un mouvement spasmodique ' spontané ' risque d'être attribué à une excitation provoquée par l'expérimentateur, s'il coïncide avec cette dernière. On saisit immédiatement la portée d'une telle confusion, si cette excitation a été appliquée au-dessus du territoire des réflexes de défense.

" D'autre part, la réflectivité peut varier au cours d'un même examen et, a fortiori, d'un jour à l'autre ; on obtient ainsi des résultats en apparence contradictoires. De plus, la surréflectivité, que nous avons en vue, n'atteint son niveau maximum qu'à une période plus ou moins tardive de l'évolution de la maladie.

" Il faut donc renouveler les explorations pendant plusieurs jours, au besoin pendant plusieurs semaines, et retenir, entre les limites variées qui ont été obtenues, celle qui est la plus élevée, qu'elle se trouve des deux côtés au même niveau ou à des hauteurs différentes, pourvu qu'elle soit dûment établie.

" Il est encore essentiel de savoir que les réflexes de défense se laissent provoquer beaucoup plus facilement sur les membres inférieurs que sur le tronc et que parfois le domaine de la surréflectivité ne dépasse pas le pli de l'aine, même lorsque la limite inférieure de la lésion siège à la partie moyenne de la moelle dorsale ou au-dessus. Notre expérience nous a appris qu'il fallait seulement tenir compte des cas où la surréflectivité envahit une partie plus ou moins étendue du tronc, à moins que d'autres symptômes ne permettent déjà de localiser la lésion dans la région lombaire ou sacrée.

" Enfin, je rappelle que les réflexes de défense se laissent provoquer de préférence tantôt par le pincement, tantôt par le froid, la chaleur, l'électricité ou la piqûre. Dans chaque cas particulier, il faut employer le mode d'excitation qui constitue le réactif le plus sensible.

" On voit, par ce qui précède, combien ces recherches sont délicates, et je conviens qu'un observateur, quelque averti et méthodique qu'il soit, ne parviendra pas toujours à obtenir de ses investigations sur les réflexes de défense des renseignements utilisables."

Il n'en est pas moins vrai, pensons-nous, que dans certains cas de compression spinale il sera possible d'acquérir ainsi des données intéressantes pour le diagnostic topographique des lésions, surtout si on les rapproche de celles, plus importantes sans aucun doute, qui sont fournies par les troubles de la sensibilité.

* * * *

Autre problème. L'intensité des réflexes de défense et les diversités de forme qu'ils présentent sont-elles en rapport avec l'intensité des lésions, le niveau où elles siègent et leur nature ? Dans mon article de 1898 j'écrivais déjà ceci à propos du signe des orteils : " Il faut donc bien remarquer que ce signe, s'il révèle l'existence d'une perturbation dans le système pyramidal, n'en dénote pas la gravité. . . . . Il semble même qu'il puisse parfois constituer le seul indice de cette perturbation." Je reviendrai dans un instant sur ce point.

Pour ce qui est relatif au niveau, j'ai dit autrefois et tous les neurologistes semblent d'accord là-dessus, que les réflexes de défense sont, d'une manière générale et sauf à la période initiale quand il y a shock, plus accentués dans les lésions spinales que dans les lésions cérébrales, ce qui tient peut-être en partie à ce que d'ordinaire les premières sont bilatérales, les secondes unilatérales.

En ce qui regarde la nature des lésions, d'après ce que j'ai observé, je pense que l'exagération des réflexes de défense est particulièrement intense et durable dans les cas de paraplégie spasmodique par compression de la moelle ou par sclérose spinale dans lesquels les altérations dégénératives du faisceau pyramidal font défaut ou sont peu prononcées. Plusieurs observations tendant à confirmer cette opinion ont été rapportées par divers auteurs [26].

Les faits de section complète de la moelle observés à la suite de traumatismes de guerre ont montré à MM. Head, Riddoch, à M Lhermitte que ces lésions, qui produisent le maximum de dégénération peuvent aussi se manifester, à une certaine période de leur évolution, par des réflexes de défense très marqués. Mais dans ces derniers cas, la phase pendant laquelle les réflexes de défense sont exagérés est relativement courte et la contracture qui se lie à ces réflexes dans la paraplégie que j'ai envisagée et dont nous aurons à nous occuper dans la suite, manque ou est peu marquée. En tout cas, mes observations ont montré que l'intensité des réflexes de défense n'est pas, tant s'en faut, en proportion directe avec le degré d'intensité de la dégénération secondaire. M. Walshe, à ce propos, dit ceci : Le point soulevé par Babinski qu'il peut n'y avoir que peu ou pas de dégénération secondaire de la voie pyramidale à l'examen anatomique dans de tels cas n'a pas de signification spéciale parceque, comme Gordon Holmes l'a montré, il n'y a pas de relation directe, constante entre la gravité des manifestations cliniques et la dégénération descendante secondaire. Une lésion en foyer de la moelle, dit-il, peut causer une paralysie spastique extrême et perte du contrôle sphinctérien, et cependant, à l'autopsie, il peut ne pas y avoir de dégénération spinale descendante.

Je sais cela depuis longtemps et j'ai précisément rapporté moi-même en 1899 une Observation de ce genre que j'ai déjà rappelée. Mais il faut savoir aussi qu'une paralysie complète due à une compression de la moelle, accompagnée de réflexes de défense très intenses, peut guérir totalement ; et cette régression des accidents n'est-elle pas expliquable par l'absence de dégénération ? C'est ce que j'ai cherché à mettre en lumière.

Je le répète, la présence de réflexes de défense même très prononcés et avec accompagnement de troubles moteurs des plus marqués, n'est pas nécessairement l'expression d'un état incurable. Entre autres faits à l'appui de cette notion, je puis vous citer quelques extraits d'une Observation publiée par Jarkowski, Lecène et moi [10] et intitulée : " Paraplégie crurale par néoplasme extra-dure-mérien. Opération. Guérison." En décembre 1911, on note ceci : " La malade présente une paraplégie spasmodique en extension avec troubles de la sensibilité remontant jusqu'à la ligne mamelonnaire. La paralysie des membres inférieurs est complète et ne cède même pas sous l'influence de divers procédés dynamogénisants (faradisation, application de la bande d'Esmarch). Cette contracture ne peut être vaincue que par un très grand effort ; pourtant, elle n'est pas toujours égale à elle-même et peut être diminuée par des mouvements passifs. De plus, la contracture en extension est entrecoupée de temps à autre par des mouvements spasmodiques involontaires qui déplacent brusquement les membres inférieurs, fléchissent la cuisse, la jambe et le pied, les allongent ensuite avec une grande force, en détachant le membre du plan du lit, et ainsi de suite, jusqu'à ce que le membre retrouve sa position primitive de repos.

" Ces spasmes se produisent soit dans un seul des membres inférieurs, soit dans les deux, et alors tantôt ils revêtent la même forme des deux côtés, tantôt ils donnent lieu à une flexion à droite et une extension à gauche ou vice-versa. Les réflexes tendineux des membres inférieurs sont nettement exagérés ; il y a de la trépidation épileptoïde du pied des deux côtés.

" On constate le signe des orteils des deux côtés.

" Les réflexes de défense sont fortement exagérés et peuvent être provoqués même par des excitations très légères. Leur forme varie suivant la position des membres et l'endroit de l'excitation, mais elle est sensiblement pareille à celle des spasmes involontaires spontanés."

La malade est opérée en janvier, 1912. L'intervention est suivie d'une amélioration qui se poursuit ensuite, mais lentement.

En juin 1914, on note : " Elle marche toute seule, sans canne, pas très vite, il est vrai, mais d'une manière à peu près normale ; elle ne traîne pas ses jambes ; elle ne fauche pas ; la pointe du pied ne butte pas contre le sol.

" Un examen objectif minutieux ne décèle comme reliquat des troubles d'autrefois qu'une tendance à l'extension des orteils et une légère exagération des réflexes de défense."

J'apprends ultérieurement que la guérison est devenue complète.

Ce n'est pas dans la patrie de l'illustre Horsley dont je m'honore d'avoir été l'ami, que je provoquerai de la surprise en rapportant l'observation d'une paraplégie due à une tumeur comprimant la moelle et guérie à la suite d'une intervention chirurgicale. Si je l'ai relatée, c'est afin de bien mettre en évidence ce fait que la surréflectivité défensive n'implique pas l'idée d'incurabilité.

Les réflexes de défense, après disparition complète des troubles moteurs, peuvent redevenir absolument normaux.

On a pris l'habitude de dire que l'exagération des réflexes de défense témoigne que la moelle est délivrée du joug des centres supérieurs ; mais, comme on le voit par ce qui précède, la moelle, en recouvrant les réflexes de défense de ses ancêtres, n'a pas reconquis toute leur indépendance ; pareille aux affranchis de Rome, elle ne jouit parfois que d'une liberté transitoire et elle est exposée à reprendre ses chaînes, ce qu'atteste le retour des réflexes à l'état physiologique.

Mais il y a plus : dans certains cas, les réflexes de défense pathologiques survivent à tous les autres troubles.

Entre autre malades de ce genre, j'en puis citer un qui, guéri d'une paraplégie par lésion syphilitique de la moelle, avait recouvré la motilité au point de pouvoir parcourir sans arrêt une distance de plus de dix kilomètres et qui cependant présentait d'une manière très nette le signe des orteils et le signe de la flexion réflexe du pied.

On peut dire qu'en pareille occurrence il s'agit de la part de la moelle d'une fanfaronnade, d'un bluff : elle affiche des airs d'indépendance, se prétend libérée, tout en obéissant servilement à l'encéphale, son maître.

Si la diminution progressive des réflexes de défense préalablement exagérés peut être un signe favorable, comme dans l'observation de tumeur que je viens de rapporter, elle peut au contraire dénoter une aggravation : dans les cas de section complète de la moelle, ces réflexes s'affaiblissent d'habitude à la période qui précède la mort.

J'ai été amené à vous indiquer l'état des réflexes de défense dans les sections spinales totales à la phase terminale, à la phase moyenne. Je dois vous exposer l'état de ces réflexes à la première phase, après le traumatisme. Sous l'influence du shock, les réflexes cutanés aux membres inférieurs peuvent être complètement abolis comme le sont les réflexes tendineux. Pour ce qui concerne les réflexes tendineux, dont je ne vous parle qu'incidemment, et contrairement à l'opinion émise par Bastian et acceptée pendant trente ans par la majorité des neurologistes, leur abolition n'est pas non plus définitive ; ils peuvent reparaître et même atteindre un degré plus élevé que la normale, mais leur retour est plus tardif que celui des réflexes cutanés. Au sujet de ces derniers, les opinions ne sont pas toutes concordantes, ce qui tient sans doute à la diversité des cas et à ce qu'un même auteur a eu seulement l'occasion d'observer un nombre de faits restreint. Il y aurait tantôt abolition du réflexe cutané plantaire, tantôt extension, tantôt flexion des orteils. D'après Guillain et Barré, le réflexe en flexion de ces paraplégiques se différencie de celui de l'homme sain par sa lenteur, son temps de latence prolongé, la persistance relative de l'attitude en flexion. Dans cette première phase, la zone réflexogène serait limitée, comme à l'état physiologique, à la zone plantaire, et ce n'est qu'ultérieurement qu'elle s'étendrait à tout le pied et à la jambe ; les réflexes deviennent de plus en plus forts et une exagération parfois très marquée des réflexes de défense se constitue alors.

Il y a lieu de comparer ces faits de paraplégie à début brusque avec les cas d'hémiplégie cérébrale succédant à un ictus apoplectique. Souvent, dès les premiers jours, alors que le malade est encore dans le coma, que la paralysie est complète et la surréflectivité tendineuse d'habitude affaiblie, on peut constater l'extension réflexe des orteils et la flexion réflexe du pied. Dans quelques cas, des neurologistes, présents à une attaque, ont eu l'occasion de constater ces signes dès la première minute. L'exagération des réflexes de défense paraît donc bien plus précoce dans l'hémiplégie cérébrale vulgaire que dans la paraplégie spinale à début brusque, ce qui dépend peut-être de ce que le shock subi par la moelle est plus grand quand il s'agit d'une lésion bilatérale que lorsqu'on a affaire à une lésion unilatérale. C'est une disposition contraire de celle qu'on observe à une période plus avancée des lésions cérébrales et spinales, ainsi que nous l'avons dit précédemment. Dans les affections spinales occupant un seul côté, la réflectivité se comporte peut-être comme dans l'hémiplégie cérébrale. J'ai rapporté un cas d'hémiplégie spinale avec anesthésie croisée due à une hémisection traumatique de la moelle, à la partie moyenne de la région dorsale, et dans lequel, quinze heures après l'accident, le côté paralysé présentait de la flaccidité, de l'irréflectivité tendineuse en même temps que le phénomène des orteils.

Je dois poursuivre l'étude des sections spinales dans leurs relations avec les réflexes cutanés, les réflexes de défense, me rapportant surtout aux travaux de MM. Head et Riddoch qui ont cherché à établir le parti qu'on pourrait tirer de l'état des réflexes de défense au point de vue du diagnostic différentiel entre les sections complètes et les sections incomplètes de la moelle. Je me permettrai toutefois de soumettre à la critique quelques-unes des idées que ces auteurs ont énoncées.

Auparavant, je dois compléter ce que j'ai dit sur les réactions obtenues par l'excitation du membre inférieur, m'étant borné d'abord, afin de ne pas compliquer mon sujet, à décrire celles qui se produisent dans le membre excité. Or, l'excitation d'un des membres inférieurs peut déterminer aussi des mouvements réflexes dans l'autre membre, que j'ai seulement notés d'une manière incidente jusqu'à présent. Je ne puis mieux faire pour vous en donner une idée que de citer un passage du travail de MM. Marie et Foix [22]. Les observations qu'ils ont faites servent de base à leur conception du mécanisme de ce qu'ils appellent "les réflexes d'automatisme médullaire."

"Nous allons voir maintenant, écrivent-ils, qu'il peut exister chez l'homme, dans quelques cas seulement il est vrai, un *réflexe d'extension croisée* analogue au "crossed extension reflex" de Philipson.

"Pour l'observer, il faut choisir un malade très spasmodique, non pas, comme nous l'avons dit, un malade atteint de paraplégie spasmodique syphilitique, mais d'une paraplégie par compression, telle que celle du mal de Pott. Nous l'avons rencontrée, en outre, de la façon la plus indiscutable, au cours de la sclérose en plaques à forme spasmodique et de la syringomyélie.

"Voici comment il faut procéder chez l'homme: on place tout d'abord les membres inférieurs en flexion légère, puis par la flexion forcée des orteils on provoque d'un seul côté le phénomène des raccourcisseurs. L'excitation doit, pour déterminer le réflexe croisé, être forte, progressive et prolongée; aussi est-il préférable de choisir des malades présentant des troubles de la sensibilité, de manière à éviter les phénomènes douloureux.

"Dans ces conditions, on voit se produire en un premier temps la flexion du membre excité, puis, l'excitation persistant toujours, se produit en un deuxième temps qui suit plus ou moins vite le premier, se confondant souvent partiellement avec lui, l'extension du membre croisé. L'ensemble reproduit, on le voit, de la façon la plus typique le 'crossed extension reflex' de Philipson."

Nous sommes maintenant en mesure d'indiquer les caractères empruntés à l'état des réflexes de défense et qui permettent, d'après Head et Riddoch, d'affirmer que la section de la moelle est soit incomplète, soit complète.

Voici les caractères qui dénoteraient une *section incomplète :*

(*a*) Présence du "crossed reflex."

Dans les sections totales, il n'y aurait pas de véritables réflexes croisés ; dans six cas sur les huit cas observés, la flexion réflexe du côté excité s'associe à une flexion du côté opposé; on peut bien observer parfois de ce côté une contraction du quadriceps et des muscles du mollet, mais sans déplacement du membre.

La proposition de Riddoch constitute non une loi, mais une règle souffrant des exceptions si l'on s'en réfère à une Observation de Lhermitte [19] et dont voici le résumé: "Syndrome de section totale de la moelle dorsale moyenne. Phase de shock durant un mois et demi. Réapparition des réflexes tendineux ; extension du gros orteil ; mouvements automatiques spontanés extrêmement intenses, mouvements de défense très vifs, mictions réflexes et spontanées, érections fréquentes ; hypersudation dans le segment inférieur du corps." Or, à la page 62, on lit ceci : "Le blessé étant dans le decubitus latéral gauche on excite la face postérieure de la cuisse droite : le membre inférieur droit se fléchit, le gros orteil s'étend ; du côté opposé le membre inférieur s'allonge, le pied s'étend et les orteils se fléchissent (Réflexes d'extension croisée)."

(*b*) Présence des réflexes en extension, qui ne s'observeraient que quand il y a persistance de l'influence des centres supérieurs. Dans la section complète, l'extension se produirait exclusivement par relâchement des fléchisseurs.

Un passage de l'Observation précédente de Lhermitte semble montrer qu'il n'en est pas toujours ainsi. A la page 63, où il est fait mention de l'état des reflexes cinquante-deux jours après l'examen précédent, nous trouvons ceci : "Les mouvements de défense sont toujours très accusés. Le pincement de la peau de la face antérieure de la cuisse détermine l'extension de la jambe et la contraction tonique du quadriceps ; quelquefois, le mouvement s'étend au membre opposé."

(*c*) Présence de ce que les auteurs anglais appellent "local sign" et qui consiste en ce que les réactions seraient différentes suivant les points excités. Si, par exemple, l'excitation de la plante du pied, selon qu'elle porte sur sa partie externe ou sa partie interne, provoque, outre la triple flexion, une abduction ou une adduction du pied, on pourrait affirmer que la section est incomplète.

D'après Riddoch, si je l'ai bien compris, dans la section incomplète, la zone réflexogène du réflexe en flexion ne dépasserait pas le genou. Cette opinion me semble en contradiction avec certains faits. Vous verrez sur un des films une malade atteinte de paraplégie incomplète ; elle peut mouvoir volontairement ses membres inférieurs et cependant l'excitation de l'abdomen avec un tube de glace provoque une flexion comme l'excitation du pied.

Par contre, on pourrait considérer, d'après MM. Head et Riddoch, comme caractéristique d'une *section totale*, d'une libération complète de la moelle, ce qu'ils appellent "Massreflex," c'est à dire réflexes, de défense toujours en flexion avec mictions réflexes et forte sudation dans le segment inférieur du corps.

J'ai eu l'occasion de décrire moi-même les troubles vésicaux en question dans mon travail déjà cité. Voici le passage qui s'y rapporte :

"Les grands mouvements des membres, qui s'imposent surtout à l'attention, furent seuls étudiés au début, mais un examen minutieux montre que d'autres groupes musculaires peuvent entrer en jeu, comme cela résulte des recherches faites par mon élève Barré. La contraction des muscles de la paroi abdominale provoque un retrait de l'abdomen ; celles des muscles de la paroi thoracique produit des spasmes respiratoires brusques. Ces divers mouvements se font généralement en même temps que ceux des membres ou les suivent à très court intervalle. Enfin, les muscles profonds du tronc, ceux qui sont en partie volontaires, comme le diaphragme, ou ceux qui sont spécialement adaptés à la vie végétative, comme les muscles intestinaux et les muscles vésicaux, peuvent également entrer en contraction en même temps que les muscles des membres ; les malades ont parfois alors des débâcles gazeuses ou des mictions involontaires qui témoignent de la mise en activité de certains de leurs muscles lisses."

Y a-t-il là des éléments de différenciation ?

Ce que je puis dire c'est que nous avons suivi très longtemps, Jarkowski et moi, un sujet atteint d'une paraplégie liée à des lésions spécifiques, paraplégie très grave, mais dans laquelle les mouvements volontaires n'étaient pas complètement abolis ; la moelle n'était donc pas entièrement libérée des centres supérieurs ; or, chez ce malade, bien souvent, des excitations diverses déterminaient, en même temps que des réflexes de défense, des mictions involontaires et l'évacuation de matières fécales.

Avant de terminer ce chapitre je ferai remarquer que l'on a très rarement l'occasion d'observer des cas avérés de section totale. Ce sont les blessures de guerre qui ont fourni le matériel d'études. Sans elle, la prétendue loi de Bastian ne serait pas encore abrogée. Mais avouez que les acquisitions neurologiques nouvelles sont une bien faible compensation des misères déchaînées par la catastrophe mondiale.

* * *

Quelques mots sur les mouvements réflexes des membres supérieurs.

Claude, dans un travail : "Sur certains phénomènes d'hyperkinésie reflexe" [13] a décrit dans l'hémiplégie cérébrale des réactions motrices réflexes et a eu surtout en vue celles du membre supérieur.

J'ai mentionné des reflexes de défense du membre supérieur dans mon article de 1915 : "Ils consistent également, disais-je, en mouvements de retrait ou d'allongement, souvent combinés à de la pronation de l'avant-bras et de l'adduction du bras. Ces mouvements peuvent présenter des modalités diverses comme les réflexes du membre inférieur, mais ils sont plus souvent que ceux-ci localisés à un seul côté."

MM. George Riddoch et Farquhar Buzzard [30] ont fait une étude approfondie de ces réactions motrices dans un travail dont j'ai donné déjà l'indication bibliographique et sur lequel le manque de temps m'empêche d'insister.

* * * *

Comment se comportent les réflexes de défense pendant le sommeil artificiel ? Cela dépend sans doute de l'agent anesthésiant dont on fait usage. On sait que l'éther agit autrement sur les réflexes tendineux que le chloroforme. Je ne puis entrer dans les détails de cette question ; je me contenterai de livrer comme document l'Observation suivante recueillie avec un soin minutieux :

Compression de la moelle de D^5 à D^6 (il s'agit du sujet que vous verrez sur un de mes films et chez lequel le niveau inférieur de la compression correspondait à la limite supérieure des réflexes de défense) : Paraplégie incomplète avec contracture en extension d'intensité moyenne. Hypoesthésie jusqu'à D^5. Réflexes rotuliens forts, trépidation épileptoïde du pied. Signe des orteils et flexion réflexe du pied très caractérisés. La malade reçoit une heure avant l'opération, en injection sous-cutanée, un centigramme de chlorhydrate de morphine et un milligramme de bromhydrate de scopolamine. Elle est ensuite endormie à l'éther avec l'appareil d'Ombredanne. L'état des réflexes tendineux et des réflexes de défense reste semblable à ce qu'il était précédemment à un moment où l'anesthésie, semblant complète, se traduit par l'abolition du réflexe cornéen, l'abolition presque complète des réflexes pupillaires, l'insensibilité au pincement avec une pince et à l'incision pratiquée pour l'intervention. Pendant vingt minutes, jusqu'au moment de l'ouverture du canal rachidien, la malade étant plongée dans un sommeil profond, les réflexes tendineux et les réflexes cutanés, examinés de deux minutes en deux minutes, ne subissent pas de modification appréciable. Je note seulement que la flexion réflexe du pied obtenue par le pincement de la peau de la jambe est particulièrement lente : le pied, après s'être fléchi, ne revient à sa position de départ qu'au bout de six à dix secondes. La contracture s'atténue progressivement.

Peu de temps après l'ouverture du canal rachidien et excision d'un tissu néoplasique un peu adhérent à la dure-mère, un nouvel examen des réflexes est fait, quatre ou cinq minutes après le précédent. Cette fois, transformation complète : tous les réflexes sont abolis. La pression artérielle qui avait été prise plusieurs fois depuis le début de l'opération et qu'on explore de nouveau à ce moment ne s'est pas modifiée : (16 avec la méthode des oscillations). Mais très peu de temps après, la pression systolique, recherchée de nouveau, n'est plus que de 5. A noter que la température rectale mesurée à ce moment est de 38°2 alors qu'elle était de 37°4 au début. Quant à la rigidité musculaire, elle a complètement disparu. En présence de cet état de shock, on met fin à l'opération. Une heure après, les réflexes rotuliens ont reparu, mais ils sont faibles ; les réflexes achilléens restent abolis ; le pincement de la peau de la face dorsale du pied ne provoque aucun mouvement ; l'excitation de la plante du pied détermine une forte extension du gros orteil, la triple flexion du pied, de la jambe et de la cuisse, et une contraction du tenseur du fascia lata. Le lendemain de l'opération le pincement du dos du pied déterminait l'extension des orteils et la flexion réflexe du pied.

* * *

Je vais actuellement étudier les réflexes de défense dans leurs rapports avec les troubles moteurs, la paraplégie spasmodique, la contracture.

Mes observations m'ont conduit à assigner à chacune de ces deux formes de paraplégie, celle en extension et celle en flexion, des caractères cliniques distinctifs, au milieu desquels les réflexes de défense occupent une place importante. Pour donner un aperçu exact des idées que j'ai exposées sur ce sujet, je pense que le mieux est d'extraire d'un travail que j'ai publié en 1912 [5], sur les réflexes tendineux et les réflexes osseux, les passages suivants :

"Je dois m'occuper, en y insistant, d'une variété de contracture sur laquelle j'ai appelé l'attention et qui, étant donné le but que nous visons, mérite d'être décrite. On l'observe surtout aux membres inférieurs et elle est un des élements constitutifs d'une espèce de paraplégie dont on saisira mieux l'aspect en la rapprochant de la paraplégie spastique d'Erb. Celle-ci, nous le rappelons, se caractérise par les phénomènes suivants : (*a*) rigidité musculaire en extension, stable ; (*b*) simple parésie, c'est à dire affaiblissement peu prononcé de la motricité volontaire ; (*c*) exagération notable des réflexes tendineux avec trépidation épileptoïde du pied, et parfois danse de la rotule ; (*d*) réflexes de défense légèrement exagérés ou à peu près normaux ; (*e*) signe des orteils.

"Voici maintenant les caractères de la paraplégie que nous avons en vue : (*a*) rigidité musculaire en flexion, qui au début cesse par moments d'une manière complète ou presque complète, mais qui plus tard devient stable ; cependant cette stabilité n'atteint guère le même degré que dans la forme précédente ; elle est sujette à des variations fréquentes qui résultent des contractions involontaires des muscles des membres inférieurs ; ces contractions sont habituellement lentes ; elles donnent lieu à des mouvements alternatifs de flexion et d'extension avec prédominance d'action des fléchisseurs ; (*b*) motricité volontaire profondément troublée ; il peut y avoir paralysie complète ; (*c*) réflexes tendineux parfois exagérés, mais pouvant être normaux, affaiblis ou même abolis ; (*d*) réflexes de défense toujours très forts ; (*e*) dans la grande majorité des cas, signe des orteils. Ajoutons que la rigidité en flexion, quand elle est devenue stable, se complique presque inévitablement de rétractions fibro-tendineuses.

"Je ne m'étendrai pas sur les lésions qui déterminent cette forme de paraplégie ; qu'il me suffise de dire qu'il s'agit généralement, soit d'altérations scléreuses diffuses de la moelle, soit d'une compression spinale par une tumeur intra-rachidienne, ou par une pachyméningite ; en outre, dans les cas de ce genre, quand ils sont très caractérisés, la dégénération secondaire des faisceaux pyramidaux fait défaut ou bien est très légère ; c'est du moins ce qui semble ressortir des observations anatomo-cliniques recueillies jusqu'à ce jour.

"Je reviens à la clinique. La rigidité musculaire de cette forme de paraplégie constitue bien une contracture ; elle est, en effet, pathologique, due à un mode de l'activité musculaire, et elle est stable, au moins à une période de son évolution. Mais, comme nous venons de le voir, cette stabilité est moindre que celle de la contracture de la paraplégie spastique d'Erb ; elle est entrecoupée en partie de contractions involontaires lentes constituant de véritables mouvements spasmodiques, et, à la phase de début, les troubles méritent moins d'être rangés dans la catégorie des contractures que dans celle des spasmes. Il en résulte que l'épithète de "spasmodique" conviendrait bien plus à cette variété de paraplégie qu'au syndrome dénommé "tabes dorsal spasmodique."

"La contracture dont nous nous occupons a pour substratum anatomique, comme nous venons de le voir, des lésions du système nerveux central ; ces lésions intéressent la voie pyramidale dont la perturbation se manifeste pendant la vie par le signe des orteils et par l'exagération des réflexes de défense.

"Me voici maintenant en mesure de répondre à la question que j'ai posée après avoir montré que la contracture vulgaire, liée à une altération de la voie pyramidale, a des relations étroites avec la surréflectivité tendineuse. Je peux affirmer qu'il existe aussi une contracture—différente, il est vrai, de la précédente par sa forme—déterminée par des lésions nerveuses centrales atteignant les faisceaux pyramidaux, et pourtant absolument indépendante de la surréflectivité tendineuse. En effet, chez les malades qui la présentent, les réflexes tendineux ne sont pas toujours exagérés, tant s'en faut ; ils sont souvent, soit normaux, soit affaiblis, soit même abolis. Les réflexes de défense, au contraire, sont non seulement toujours présents, mais ils atteignent une très grande intensité.

"Mes observations ont été confirmées sur tous les points par plusieurs neurologistes.

"Cette forme de contracture, surtout commune aux membres inférieurs, peut atteindre en même temps les membres supérieurs, où elle offre les mêmes caractères : rigidité avec mouvements spasmodiques, affaiblissement ou abolition possible des réflexes osso-tendineux, réflexes de défense très forts.

"Qu'on la considère aux membres inférieurs ou aux membres supérieurs, ce qui frappe surtout, ce sont ses liens intimes avec les réflexes cutanés de défense dont elle parait dépendre, comme la forme habituelle de la contracture dépend de la surréflectivité tendineuse. Pour mettre ces traits en évidence et pour donner à chacune de ces formes de contracture—qui peuvent d'ailleurs s'associer—une dénomination qui la distingue, j'ai proposé d'appliquer à l'une le qualificatif de *tendino-réflexe* et celui de *cutanéo-réflexe* à l'autre."

A côté des formes types, il y a des formes qu'on pourrait appeler intermediaires où l'on trouve les principaux caractères de la contracture cutanéo-réflexe (motricité volontaire très troublée, réflexes de défense très forts) bien que les membres inférieurs gardent d'habitude une attitude en extension. Précédemment, j'en ai montré un bel exemple en vous relatant l'Observation d'une paraplégie due à une compression par tumeur et guérie à la suite de l'intervention chirurgicale. Cette dernière forme comporte un pronostic moins sévère que la paraplégie spasmodique en flexion, laquelle correspond à un stade plus avancé de l'affection.

En France, ma manière de voir a été généralement acceptée et dans un article récent M. Foix [16] écrit ceci :

" *Contracture d'automatisme médullaire.*—C'est à mon maître Brissaud, dont la mort prématurée fut un deuil pour la neurologie française, que revient l'honneur d'avoir étudié en premier les contractures en flexion ; mais c'est M. Babinski qui le premier en a établi toute l'importance en montrant qu'elles avaient une séméiologie, une signification pathologique complètement différentes des contractures en extension.

" C'est en effet au sujet des paraplégies en flexion que M. Babinski a établi une distinction entre les contractures tendino et cutanéo-réflexes qui marque une date dans l'histoire des contractures.

" Nous ne chicanerons pas ici M. Babinski sur le mot plus ou moins heureusement choisi de cutanéo-réflexe. Il est évident que cette contracture n'a rien de cutané, puisque les réflexes qui la caractérisent peuvent être aussi bien provoqués par l'excitation de la sensibilité profonde que par celle de la sensibilité superficielle. Il n'en est pas moins vrai que la contracture en extension est avant tout caractérisée par l'exagération des réflexes tendineux et la faible intensité des réflexes d'automatisme appelés encore de défense. Tandis que la contracture en flexion est caractérisée non seulement par l'exagération considérable des réflexes d'automatisme, mais encore par la diminution ou l'abolition des réflexes tendineux.

" A cette différence de séméiologie répondent des différences profondes d'étiologie, de pronostic, de signification physiologique.

" Voici une malade qui présente précisément cette contracture en flexion. Considérons-la un instant. Nous voyons d'abord quelle est son attitude. Ses jambes sont ramassées vers elle. Examinons-la de plus près. C'est une attitude de raccourcissement. Et ce raccourcissement comporte le triple retrait segmentaire que nous avons déjà deux fois rencontré : flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin.

"Poursuivons plus loin notre étude. Les réflexes rotuliens sont faibles, il n'y a pas de clonus du pied. Par contre, ces réflexes d'automatisme sont très faciles à provoquer : voici le phénomène des raccourcisseurs, une ébauche de réflexe d'allongement, un réflexe partiel d'allongement croisé. C'est bien la dissociation décrite par M. Babinski.

"Comment peut-on interpréter cette séméiologie d'abord, cette attitude ensuite ?

"En ce qui concerne les réflexes d'automatisme, leur intensité implique une libération de la moelle inférieure. C'est là un fait qui n'est pas sans importance, car il indique en général des lésions plus profondes que celles qui s'accompagnent de contractures en extension. On voit assez souvent la contracture en flexion se substituer à la contracture en extension. Pendant quelque temps alors, il y a lutte entre les deux tendances et les deux réflectivités. Toujours la victoire de la flexion implique une aggravation de l'état du malade.

"Y a-t-il seulement *libération* de la moelle ? N'y a-t-il pas en outre irritation, *exaltation* de l'automatisme médullaire ? C'est une chose que, pour ma part, je crois, mais il est difficile d'en donner la preuve."

. . . . .

"Quant à la contracture en flexion elle-même, son aspect indique quelle en est la pathogénie. Elle n'est autre chose, en effet, qu'un phénomène des raccourcisseurs fixé."

Sauf sa remarque sur le terme cutanéo-réflexe, M. Foix est à peu près d'accord avec moi. Je ne trouve pas, soit dit en passant, que son objection soit juste : peu importe que les réactions motrices puissent être obtenues aussi par l'excitation des parties profondes ; il suffit que l'excitation de la peau seule puisse y donner naissance pour qu'on ait le droit de dire qu'elles sont cutanées. Mais c'est là un point tout à fait secondaire. Pour le fond de la question, M. Foix confirme mes observations.

Au contraire, les neurologistes anglais, en particulier MM. Walshe et Riddoch, expriment des critiques qui sont peut-être, au moins en partie, la conséquence de malentendus. Si je saisis bien ce qu'il y a de principal dans les idées de M. Walshe sur les réflexes d'extension et de flexion, voici en quoi elles consistent :

Les extenseurs et les fléchisseurs forment deux groupes soumis chacun à une forme spécifique d'activité réflexe ; elle est tonique dans l'un, clonique, phasique, dans l'autre. Le centre de cette activité a pour siège unique les noyaux spinaux, en ce qui concerne les fléchisseurs : l'activité des extenseurs nécessite, pour se maintenir, la mise en jeu d'un autre appareil réflexe dont le centre occupe le mésocéphale, les noyaux paracérébelleux probablement (centre des réflexes de posture).—Une lésion cantonnée dans le faisceau pyramidal exalte à la fois l'activité réflexe des extenseurs et celle des fléchisseurs et donne lieu à une paraplégie en extension. Une lésion siégeant au-dessus du mésocéphale ne produirait jamais une paraplégie en flexion.—Au contraire, une lésion de la voie pyramidale associée à une lésion occupant une des parties de l'arc réflexe, ayant pour centre les noyaux paracérébelleux, détermine une paraplégie spasmodique en flexion ; en effet, l'activité réflexe des fléchisseurs n'est pas affectée par l'interruption de cette voie puisque cette activité est d'origine uniquement spinale ; elle est même augmentée, n'étant plus freinée par une force antagoniste. De pareilles altérations donneraient lieu à une exagération des réflexes s'opérant toujours en flexion ; l'extension, quand elle s'observe, n'étant qu'un effet du relâchement des fléchisseurs, ou étant un allongement croisé, toujours secondaire, jamais primitive.—Les réflexes de défense sont d'autant plus forts (période de shock mise à part) que la séparation entre les centres spinaux et les centres mésocéphaliques est plus grande, que la libération de la moelle est plus complète.—Mais, pour qu'il se développe de la contracture, il faut que les muscles aient un certain degré de tonicité que n'atteignent pas, même après la période de shock, les muscles dans les cas de paraplégie consécutive à une section totale de la moelle ; la contracture implique la persistance de quelques connexions entre l'encéphale et la moelle.

A certains points de vue, cette conception pathogénique cadre avec la description clinique que j'ai faite antérieurement de la paraplégie en extension et de la paraplégie en flexion.

Mettons en regard les caractères symptomatiques tracés par moi de ces deux types de paraplégie et les données physio-pathologiques énoncées par les auteurs anglais.

PARAPLÉGIE SPASMODIQUE EN EXTENSION.

(*a*) Stabilité de la contracture.	L'activité réflexe des extenseurs est à forme tonique.
(*b*) Réflexes de défense légèrement exagérés ou à peu près normaux.	L'activité réflexe des fléchisseurs a pour antagoniste celle des extenseurs.

PARAPLÉGIE EN FLEXION.

(*a*) Instabilité relative de la contracture avec variations fréquentes liées à des mouvements alternatifs de flexion et d'extension et avec prédominance d'action des fléchisseurs.	L'activité réflexe des fléchisseurs est à forme clonique phasique.

(*b*) Exagération notable des réflexes de défense.	L'activité réflexe des fléchisseurs n'est plus freinée par une force antagoniste.
(*c*) Motricité volontaire profondément troublée.	Les réflexes de défense sont d'autant plus forts que la libération de la moelle est plus complète.
(*d*) Les dégénérations secondaires peuvent être très faibles ou nulles.	Pour que la paraplégie en flexion avec contracture se développe, les connexions entre la moelle et l'encéphale ne doivent pas être complètement rompues.

Mais il est certain qu'il y a aussi des divergences pouvant résulter de ce que le sens des termes employés n'a pas été suffisamment précisé. Il me semble que MM. Walshe et Riddoch, tout en reconnaissant l'intérêt qu'il y a à distinguer la paraplégie en extension de celle en flexion et en rappelant mes travaux sur cette dernière, n'ont pas bien saisi mes idées et qu'il y a là une confusion. Pour eux, la paraplégie spasmodique en flexion est réalisée quand à une paraplégie, serait-elle flasque, s'associent des réflexes de défense amenant la triple flexion, et c'est dans les cas de section complète de la moelle qu'on en observerait les exemples les plus typiques. Or, dans ma description de la paraplégie en flexion, j'ai fait intervenir l'élément *raideur* (contracture cutanéo-réflexe) ; cette rigidité, il est vrai, peut céder par moments au début ; mais plus tard elle devient relativement stable. C'est ce type que j'ai toujours eu en vue, celui d'ailleurs que d'autres neurologistes ont observé après moi et qu'on rencontre encore assez souvent dans la pratique habituelle, les cas de section totale étant tout à fait exceptionnels.

J'estime être en droit de maintenir mon opinion suivant laquelle ce type de paraplégie en flexion, avec contracture, réflexes de défense extrêmement exagérés, exagéres au maximum, est d'habitude liée à des compressions, des lésions scléreuses diffuses sans dégénération secondaire ou avec dégénérations secondaires minimes, ce qui ne veut pas dire que cet état soit incompatible avec des dégénérations secondaires marquées. A cet égard, les observations nouvelles, de guerre, si intéressantes qu'elles soient, n'infirment aucunement les observations anciennes.

Contre l'opinion de M. Walshe et de ceux suivant lesquels une lésion siégeant au-dessus du mésocéphale ne produirait jamais une paraplégie en flexion, on peut faire valoir l'Observation rapportée par MM. Pierre Marie et Foix [24] et intitulée : " Paraplégie en flexion d'origine cérébrale par nécrose sous-épidymaire progressive."

"Notre cas, disent les auteurs, est, croyons-nous, le premier cas anatomo-clinique de paraplégie en *flexion* d'origine cérébrale ; en tout cas, le premier dans lequel on ait observé la dissociation signalée dans certains cas par M. Babinski entre les réflexes d'automatisme dits de défense et les réflexes tendineux.

"Ceci est une notion importante au point de vue physiologique, car il n'existait pas chez notre malade de lésions mésocéphaliques, mais simplement une double lésion cérébrale. La suppression de l'influence des centres mésocéphaliques n'est donc pas indispensable pour que se produise l'automatisme médullaire et la paraplégie en flexion. Il n'est pas nécessaire non plus qu'il y ait lésion irritative comme dans le cas déjà signalé de M. Babinski (paraplégie en flexion par compression mésocéphalique) ; une simple lésion destructive suffit, en supprimant l'influence cérébrale."

A ce sujet, je rappellerai que dans mon travail de 1911 sur la Paraplégie spasmodique avec contracture en flexion, j'écrivais ceci, p. 135 : "Des lésions bilatérales de l'encéphale semblent pouvoir donner naissance à un syndrome analogue" [3].

Il faut s'attendre à la publication de nouvelles observations et à de nouvelles discussions. Le dernier mot sur cette question ne paraît pas avoir été dit.

* * * *

Dans une communication intitulée : "De la surréflectivité hyperalgésique" [8], nous avons relaté, Jarkowski et moi, trois Observations de Syndrome de Brown-Séquard, dans lesquelles nous avons été frappés par la présence d'un même phénomène dont voici les traits essentiels : une excitation telle que le pincement de la peau du côté de la lésion, où il y a de l'hyperalgésie, sans être suivie d'aucune manifestation de ce côté, donne lieu du côté opposé à une réaction motrice brusque, en même temps qu'elle détermine des grimaces et une inspiration bruyante (phénomènes analogues aux "pseudaffective reflexes" observés par Sherrington chez les animaux décérébrés).

Dans un travail ultérieur, "Automatisme et hyperalgésie dans l'hémiplégie cérebrale" [9], nous avons relaté les faits suivants : chez certains hémiplégiques présentant de l'hyperalgésie, l'excitation des téguments du membre inférieur est suivie d'une réaction motrice du membre supérieur du côté sain, différente suivant qu'on excite le côté sain ou le côté malade. Dans le premier cas, la main se porte sur le point excité comme pour le protéger. Dans le deuxième, le membre supérieur se soulève, la main se porte sur la tête et vient s'appliquer soit à sa partie antérieure, soit à sa partie postérieure. Dans certains cas, nous avons été frappés par la constance avec laquelle ces réactions se produisaient. On pouvait à volonté, en pinçant alternativement les deux côtés, faire exécuter à la main saine des mouvements en sens inverse : la main était-elle appliquée sur la tête à la suite du pincement du côté malade, on obtenait son déplacement vers le membre inférieur du côté sain en pinçant la jambe saine ; et si alors on pinçait la jambe du côté malade, le bras s'élevait de nouveau et la main se portait sur la tête.

Ces réactions motrices diffèrent cliniquement de celles que nous avons étudiée dans notre Conférence. Nous les rapprochons des réflexes de défense, mais nous les en distinguons. Les unes et les autres peuvent d'ailleurs être associées.

Nous pensons que les réactions observées chez les malades qui font l'objet de notre travail sur la réflectivité hyperalgésique sont des réflexes ayant leur centre dans l'encéphale.

Quant aux mouvements de la main vers la tête constatés chez les hémiplégiques dans notre Note sur l'automatisme et l'hyperalgésie, nous sommes portés à croire qu'il s'agit là d'un acte automatique déclenché par la sensation spéciale qui résulte de l'hyperalgésie, sensation nouvelle, non encore éprouvée, insolite et occasionnant ainsi une surprise, un état d'anxiété que traduit la physionomie du malade, bien que sa conscience puisse être considérablement amoindrie.

Nous avons cru devoir signaler ces phénomènes dont on trouvera la description détaillée dans nos publications. Mais nous n'y insisterons pas davantage, faute de temps et parceque, en le faisant, nous sortirions des limites de notre programme.

* * * *

Je me suis proposé de traiter dans cette Conférence la question des réflexes de défense surtout en clinicien, en neurologiste. Je ne crois pas cependant pouvoir la terminer sans vous dire quelques mots du mécanisme de ces réflexes, dont il a été déjà question, du reste.

Vous avez vu que MM. Marie et Foix ont insisté sur la présence des réflexes d'extension croisée observés par eux chez certains sujets atteints de lésions de la voie pyramidale. Les rapprochant du " crossed extension reflex " de Philipson, ils arrivent à cette conclusion que les mouvements réflexes dits de défense sont des mouvements du même ordre que les mouvements du stepping reflex et constituent des manifestations de l'automatisme spinal de la marche. Les neurologistes anglais contestent l'exactitude de cette conception ; ils soutiennent que chez l'homme, dans les sections totales de la moelle, les excitations nociceptives d'un côté, quand elles provoquent l'activité des extenseurs du côté opposé, ne donnent lieu qu'à des contractions légères sans déplacement des divers segments du membre, et que les mouvements alternatifs rythmés qu'on observe chez le chien spinal font ici défaut.

M. Foix, dans une publication récente à laquelle j'ai déjà fait des emprunts, semble faire quelques concessions tout en maintenant en grande partie son opinion première. "Il est possible, dit-il, que l'automatisme de défense entre pour une part dans la pathogénie de ces réflexes, mais, pour la majeure part, ils se rattachent à l'une des fonctions essentielles de la moelle, c'est à dire à l'automatisme de la marche."

J'ai cherché précédemment à faire ressortir la distinction capitale qu'établissent les auteurs anglais entre le groupe des fléchisseurs et celui des extenseurs soumis chacun à une forme spécifique d'activité réflexe : les réflexes d'extension seraient des réflexes de posture ; les réflexes de flexion seraient des reflexes cloniques, phasiques. C'est dans le groupe de ces derniers réflexes que rentrent pour la plus grande part ce qu'on appelle les réflexes de défense.

La conception fondamentale des neurologistes anglais, issue des idées de Jackson, de Sherrington, est que ces réflexes de flexion tels qu'on les observe à l'état pathologique traduisent la libération de la moelle par rapport aux centres supérieurs.

Les faits observés cadrent fort bien pour la plupart avec cette conception. Toutefois, sans en contester la justesse, on peut se demander si, dans la genèse des phénomènes en question, l'élément "irritation" ne peut pas jouer aussi un certain rôle.

C'est une idée que M. Foix tend à admettre, comme on l'a vu précédemment.

Ce fait que les réflexes de défense m'avaient paru dès mes premières observations particulièrement intenses dans les cas de compression de la moelle et de sclérose spinale sans dégénération secondaire m'avait déjà conduit autrefois à cette même idée.

A l'appui de cette manière de voir on peut invoquer encore d'autres faits sur lesquels nous avons déjà insisté. On peut observer parfois—nous le rappelons—des sujets atteints de lésions spinales qui, après avoir présenté une paraplégie plus ou moins marquée, paraissent complètement rétablis : la motricité est redevenue normale, la sensibilité est intacte, il n'y a pas de perturbation des sphincters, et cependant il y a persistance très nette du signe des orteils et de la flexion réflexe du pied. Sauf ces derniers phénomènes, le fonctionnement du système nerveux semble absolument normal. Est-il permis de soutenir en pareil cas qu'il y a libération de la moelle ? Ce ne serait alors qu'une libération relative aux reflexes de défense. L'état pathologique de ces réflexes ne se comprendrait-il pas mieux dans des cas de ce genre si l'on admettait qu'il est sous la dépendance de l'irritation des centres nerveux produite par le reliquat de la lésion ?

Considérant maintenant la question d'un autre point de vue, je soumettrai quelques idées à vos réflexions.

Au début de cette Conférence, j'ai tracé un parallèle entre les réactions motrices consécutives aux excitations périphériques suivant qu'elles sont pathologiques ou physiologiques. Il résulte de ce que j'ai dit que les premières peuvent être considérées comme l'exagération des secondes, ou plutôt les secondes comme la réduction des premières : de part et d'autre, en effet, on observe le phénomène de la triple flexion avec contraction du tenseur du fascia lata ; mais ce qu'il y a de spécial aux réactions physiologiques c'est qu'on ne les obtient que par l'excitation de la zone plantaire et que les mouvements sont plus rapides et moins amples. A l'état pathologique, la triple flexion (seul mode de réaction que j'envisage ici) semble bien pouvoir être interprétée comme un retour à un état ancestral : la partie excitée fuit l'objet vulnérant (retrait du membre, raccourcissement) et une excitation peut déterminer, loin du point où elle a eu lieu, un mouvement de fuite ; c'est ainsi que la triple flexion peut être provoquée par excitation de l'abdomen ou du thorax. A l'état physiologique, ces réactions ancestrales se sont maintenues, mais ont subi des modifications importantes. Comment le comprendre? On pourrait dire que lorsque les centres supérieurs ont asservi les centres inférieurs, ceux qui correspondaient aux centres spinaux, ils ont inhibé les réactions susceptibles d'être nuisibles à l'individu et ont laissé subsister, en les adaptant à ses besoins, celles qui sont capables de lui servir. Or, il est evident que la triple flexion consécutive à une excitation de la jambe, de la cuisse ou de l'abdomen ne pourrait avoir que des inconvénients ; cette réaction a donc été supprimée. Que sous l'influence d'une irritation nocive de la plante du pied continuellement en contact avec le sol, la triple flexion s'opère, même indépendamment de la volonté, cela ne peut être qu'utile ; cette réaction a donc été conservée. Mais il y a intérêt aussi, au point de vue de la marche, à ce que la réaction ne soit pas de longue durée ; aussi la décontraction est-elle rapide au lieu d'être lente. On saisit ainsi les raisons pour lesquelles, à l'état physiologique, les réactions motrices qui me paraissent ressortir aux réflexes de défense, s'effectuent avec rapidité et ne se produisent que lorsque les excitations portent sur la région plantaire.

Il me semble intéressant de rappeler à ce propos que dans les sections totales de la moelle, après la période de shock, lorsque les réflexes cutanés reparaissent. la région plantaire est seule réflexogène pendant un certain temps.

Comparons maintenant le réflexe des orteils aux réflexes précédents. Si à l'état pathologique la réaction habituelle des orteils, l'extension, peut être rapprochée, en ce qui concerne son mécanisme, de la triple flexion, à l'état physiologique le mouvement des orteils, la flexion, semble avoir une autre signification que la triple flexion du pied, de la jambe et de la cuisse. M. Riddoch fait observer que la flexion réflexe des orteils fait partie du stepping-reflex, et qu'elle accompagne l'extension de la cuisse, de la jambe et du pied. Mais il est à remarquer qu'à l'état physiologique chez l'homme, l'excitation de la plante du pied, qui provoque la flexion des orteils, détermine du même côté la triple flexion du membre inférieur et il en résulte une quadruple flexion. Cette flexion des orteils ne serait-elle pas aussi le témoin d'une réaction ancestrale, ayant apparu toutefois à une période du développement plus avancée que les réflexes de défense dont il a été précédemment question, période où les orteils servaient de griffe ? Cette réaction avait aussi en partie la protection pour but, mais c'était un mode de protection différent de celui qui est réalisé par les réflexes de défense primitifs ; il ne s'agit plus d'une fuite localisée, d'une retraite en face d'une offensive ; ce mouvement de griffe vis à vis d'une aggression constitue une contre-offensive, mode de protection d'un ordre plus élevé ; on conçoit du reste fort bien qu'un animal cherchant à se défendre combine l'attaque avec la fuite. On saisirait ainsi la quadruple flexion à l'état physiologique : la flexion de la cuisse, de la jambe et du pied ressortissant aux réflexes de défense primitifs, la flexion des orteils étant l'expression atavique d'un réflexe de préhension.

Cette conception permettrait de comprendre pourquoi l'extension des orteils n'est pas toujours associée à la triple flexion ; suivant que dans le domaine des orteils, le réflexe de fuite l'emportera, ce qui est la règle à l'état pathologique, sur ce que nous appelons le réflexe de préhension, ou bien sera dominé par lui, on obtiendra l'extension ou la flexion des orteils.

Je rappellerai à ce propos que M. van Woerkom, dans le travail cité plus haut, fait ressortir que " le gros orteil est construit dans certains stades de la vie intra-utérine pour remplir une fonction de préhension." Cet état qui chez les autres primates est perpétuel, est passager chez l'homme.

Est-il nécessaire d'ajouter qu'il s'agit là pour une grande part d'hypothèses !

* * * *

Dès le début de mes recherches sur le phénomène des orteils, j'avais eu l'occasion de le constater chez des nourrissons, et il m'avait semblé qu'il persistait approximativement jusqu'à la période où l'enfant commence à marcher, ce qui s'explique quand on se rappelle quel est l'état du système pyramidal à cette époque de la vie : on peut dire que l'enfant est atteint d'une paraplégie—curable—comme on peut dire aussi que chez lui la moelle n'est pas encore sous la domination de l'encéphale.

D'après Léri [20], à la naissance l'extension des orteils est la règle ; la flexion l'exception. L'extension disparaît en général, chez l'enfant normal, vers 5 ou 6 mois, mais il y a des variétés individuelles ; il peut y avoir une période de transition assez prolongée, marquée par des alternatives de flexion et d'extension et souvent par l'extension unilatérale.

Des recherches nouvelles de Bersot [12], de Lantuejoul (communication orale) ont montré qu'il y avait lieu de rectifier un peu les données précédentes : à la naissance, puis pendant un laps de temps d'une durée assez courte, les orteils réagissent en flexion et ce n'est qu'ultérieurement que l'extension apparaît. Cela surprend d'abord, mais n'est pas contradictoire si l'on admet que la flexion des orteils, réaction physiologique il est vrai, est le reliquat d'une réaction ancestrale et si l'on se rappelle que chez l'adulte on peut observer un réflexe en flexion chez des sujets atteints de lésions avérées de la voie pyramidale.

En ce qui concerne la flexion réflexe du pied, on la constate aussi chez l'enfant, ainsi que l'a établi une de mes élèves, Mlle Rosenblum, qui a fait de cette question l'objet de sa Thèse inaugurale ; mais l'extension du gros orteil subsiste d'habitude plus longtemps que la triple flexion.

Je vous signale avant de terminer un travail de M. Minkowski ayant pour titre : " Sur les mouvements, les réflexes et les réactions musculaires du fœtus humain de 2 à 5 mois, et leurs relations avec le système nerveux fœtal " [25].

J'extrais de cet article (p. 1113) le passage suivant : " On peut dire en général que chaque partie des téguments peut servir de zone réflexogène à des réactions motrices très variables, proches et lointaines, ayant la tendance à se généraliser plus ou moins à tout l'organisme fœtal."

Cette donnée est à rapprocher de ce que nous avons dit précédemment sur la possibilité de provoquer parfois, à l'état pathologique, des réflexes des orteils et du pied en excitant les téguments de l'abdomen et du thorax.

Messieurs, comme vous venez de le voir, l'étude des réflexes de défense soulève des problèmes de phylogénie et d'ontogénie, et à cet égard elle est déjà fort intéressante ; mais elle l'est surtout pour le neurologiste. Ces réflexes constituent un chapitre important de la pathologie du système nerveux.

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A STUDY OF THE SHERRINGTON DECEREBRATE ANIMAL IN THE CHRONIC AS WELL AS THE ACUTE CONDITION.

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[1] In general the experimental work was done by H. C. B., and Chapters II, III and VI (*b*) were written by him. The semi-decerebrations and all the anatomical examinations were made by W. G. P., and Chapters IV, V and VI (*a*) were written by him.

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INTRODUCTION.

THE researches on which this paper is based were commenced originally in a search for a preparation which would allow experiments on the origin of surgical shock, and also on the effect of temperature on the resistance to infection in animals not under an anæsthetic and yet without there being any possibility of pain. The Sherrington preparation seemed ideal for this purpose, since the question of any conscious sensation could be completely excluded, and in addition the preparation would remain quiet during experimentation. The main object has, therefore, been to develop a technique which would allow the preservation of the decerebrate animal for many days, in spite of the removal not only of the cerebrum, but also of the basal ganglia and most of the mid-brain. This has necessitated the use of 124 animals, and in the course of the work some points of interest have arisen in connection with the reflexes and the histological anatomy. In many experiments our data are not as complete as we would have wished, but it was found that the process of examining the animals diminished their chance of survival and consequently the observations had to be curtailed, if the main object of the research was to be attained.

In spite of these difficulties a certain number of important facts were demonstrated. One of the most noticeable was the very remarkable similarity between the decerebrate preparations which had been kept "alive" for two or three weeks, and the acute preparations described by Sherrington on examination an hour or so after the operation. The decerebrate rigidity often continues (with only brief intermissions) for weeks, so that there can be no possibility of the condition being due to stimulation of the cut nerve fibres at the site of operation, and since in this time the damaged nerves are undergoing degeneration it is possible to exclude definitely some structures from any participation in this reflex. On the other hand, the chronic preparations do show certain definite differences from the acute; for instance, after the first two or three days a small percentage of the animals will occasionally make definite sounds, and these sounds appear to be reflex since they occur usually as the result of some definite stimulus. The most common of these sounds was purring occurring immediately after the stomach had been filled with milk by a stomach tube, while mewing has only been observed in two animals, and in these it occurred only once or twice and could not be made to recur by applying stimuli which would be painful to a conscious animal.

Extensive histological studies have only been possible on a few of the preparations, but in these the results are of interest since we believe that never before have preparations been maintained in a sort of life so as to allow degeneration to occur after such complete removal of all the higher nervous centres. In many other cases the nervous tissue was useless for detailed examination as the result of incubation for some hours after death and consequent rapid post-mortem changes.

CHAPTER I.—HISTORICAL NOTE ON DECEREBRATION.

The method of removing parts of the brain in order to study function in the central nervous system has been employed since Rolando's experiments on birds in 1809. Flourens, indeed, succeeded in keeping pigeons alive for months after the removal of the fore-brain. But Longet [32], in 1842, first discriminated carefully as to what brain structures he actually removed. He noticed that many "reactions" remained if he removed all of the brain down to and including the colliculi—"chose remarquable!"; but that after removal of the pons all reactions disappeared, excepting only respiration and circulation.

Goltz kept three decerebrate dogs alive for months. The brain-stem of one animal most carefully studied was examined by Gordon Holmes [21], who found that a considerable amount of thalamus and all the cranial nerves were intact, although there seemed to be some softening of the corpora quadrigemina. There was no loss of temperature control and the animal shivered in a cold room. It could walk and would eat when brought close to food. Rothmann [51] [52] likewise produced a chronic preparation, a dog from whom all or most of the brain above the optic thalamus was removed. This animal ate and drank normally, walked and ran and showed a limited ability to learn. He likewise had normal temperature control and apparently normal muscle tone. Karplus and Kreidl [25] extirpated the hemispheres of monkeys and kept one alive as long as twenty-six days. More recently, Dusser de Barenne [2] has kept one cat alive six months, and another animal eleven months, after removing the fore-brain. A careful examination by Brouwer [7] of the post-mortem material showed the thalamus, mid-brain, and rhinencephalon to be intact in one, and most of the thalamus and mid-brain in the other. These preparations did not show decerebrate rigidity and were able to maintain a normal temperature. Only the animal with a portion of the fore-brain intact would eat spontaneously.

As indicated briefly above, in all previous *chronic* decerebrate preparations much of the thalamus was intact as well as the mid-brain. The animals possessed normal temperature control and have been able to execute complicated co-ordinated movements.

Decerebration at the level of the mid-brain was shown by Sherrington in 1896 to produce "decerebrate rigidity." This condition in *acute* preparations has been the subject of much study since that time by Horsley, Thiele, Weed, Magnus, Cobb, *et al.* Their conclusions will be discussed in another part of this communication. Recently, signs and symptoms in a group of patients considered to be analogous to decerebrate animals have been described by Wilson [63]. Riddoch and Buzzard [49] have also described such symptoms in man.

Boyce [6], in 1895, removed the brain on one side down to the middle of the mesencephalon and kept the animals (cats) alive as chronic preparations. His principal interest was in the descending degenerations thus produced. Probst [46], in 1904, made sections through one lateral half of the mid-brain without removing any tissue and studied the general behaviour of the animals as chronic preparations.

This brief sketch makes no pretence to enumeration of all of the valuable contributions to neurology made by this experimental method. In general, preparations produced by decerebration at higher levels and extending down as far as the medulla oblongata have been studied as *acute* experiments. In the case of all previous *chronic* experiments, the level of removal has been at least well above the mid-brain and most of the thalamus.

CHAPTER II.—TECHNIQUE.

The animals used have been cats in all cases. The general procedure has been to decerebrate the animals aseptically under an anæsthetic and then to keep them under conditions which will maintain by artificial means their temperature constant. In the main the technique has followed the lines described by one of us (H. C. B.) [4] in a preliminary communication,[1] but as it has been modified in details it will be advisable to give here a full description. The whole process is founded on Sherrington's original (and older) method developed in 1896 [53] [54].

(*a*) *Operative.*

Pure chloroform has been used as the anæsthetic since we have had no success with ether. The preparations have considerable difficulty in getting rid of mucus and this probably accounts for the difficulties we have had. Subcutaneous injection of 0·5 mgm. of atropine has been given immediately after induction of anæsthesia in some animals, perhaps with beneficial effect. During the actual decerebration a total cessation of respiratory movements for a short while is not uncommon, and causes the loss of some animals. To overcome this intratracheal insufflation has been tried both with chloroform and ether. With chloroform insufflation we have had some success, but the greater irritation to the trachea and the consequent risk of infection seem to more than counterbalance the diminished risk of the actual operation. Cessation of respiration is less liable to occur if the animal is deeply anæsthetized at the time the section is made, so that with a good anæsthetist trouble of this kind is rare, even with an ordinary inhalation method, and it is this that we have mostly used.

The skin on the back of the head is shaved, cleaned and painted with an alcoholic solution of iodine, and in the later technique the animal is then turned over and the front of its neck is also shaved. A small incision is made (1 to 2 cm. in length) in the mid-line at the level of the thyroid cartilage, and from this both carotid arteries can be reached; a thick ligature is passed around each of them, and is then tied to form a loop so that traction can be made on the vessels to obstruct the blood-flow as desired. These two loops are brought out through the middle line and then the wound is closed with two or three waxed silk sutures. Hæmostat forceps hanging on these loops during the actual process of decerebration will prevent most of the bleeding and allow much more accurate work. It does not seem necessary to take any aseptic precautions after this neck wound has once been stitched up, and we have had no serious infection of these wounds.

The animal is then again turned over and an incision made on the back of the head. A skin flap is turned back on one side, the temporal muscle is separated from the bone, the skull is trephined and the hole enlarged to a good size. While the actual decerebration is performed the weights on the carotid are allowed to hang free and constrict the vessels and the anæsthetist compresses the vertebral arteries just below the transverse processes of the atlas. The dura is opened and with a blunt spatula the occipital lobe on the near side is removed so as to bring into view the corpora quadrigemina. The division across the brain-stem can then be made at any desired level; this is done with the same blunt spatula, carrying the cut right through the brain to the base of the skull. It has proved much more satisfactory to make absolutely certain of preserving the pituitary gland intact, as will be explained later, and this has been attained most easily by the careful choice of the plane of the section and by carrying a horizontal cut forwards with a specially bent and rather blunt scalpel, starting from the transverse incision and passing forwards through the base of the brain a millimetre or two above the level of the pituitary. The whole of the brain matter above these two cuts is then scooped out and the cavity is lightly plugged with cotton wool. After this the vertebral arteries may be released and a little later the carotid blood-flow may be allowed to return. The whole procedure of removing the brain should only take about a minute or two.

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[1] In the protocols "earlier method" indicates that the operation was performed as described in this communication.

The packing in the cavity is left for five or ten minutes and is then carefully removed. If there is any bleeding a small pad of muscle is put over it and packing is repeated and maintained for another five minutes. When the cavity is quite dry the closing of the wound is commenced. It is important to obliterate the large dead space of the cranial cavity in order to minimize the chance of infection. This has been done usually by filling it with a mixture of equal parts of vaseline and paraffin wax (melting 55° C.), the mixture setting at about 45° C. It is sterilized by heating to 140° C. for three-quarters of an hour on three successive days. If the hæmorrhage has been difficult to stop it is usually safer first to spread over the base of the skull a thin layer of gauze soaked in saline, the end of the gauze protruding through the wound, the temporal muscle being split vertically so as to make this easier, and then pour in the wax at a temperature of about 47° C., allowing it to set in the cranium. The wax does not stick to the wet gauze, so that when the wax is set the gauze may be gently withdrawn, or if hæmorrhage is feared it may be left in place until the following day. In the latter case a corner of the gauze may either be allowed to protrude through a counter-incision in the skin, or it may lie just beneath the skin which has been closed by a suture above it, so that on the next day the stitch may be removed and the gauze withdrawn without any trouble. It is probable that it is best to leave always a little gauze in place while the wax is setting, since on removal it leaves a small cavity and so allows room for some swelling of the remaining parts. In the earlier experiments where the whole brain matter to the level of the tentorium was scraped away trouble from this factor was not conspicuous, but with the modification of the operation as here described a post-operative rise in intracranial pressure may play a more important rôle.

In the few animals in which only one hemisphere has been removed the use of wax has proved unsatisfactory, probably owing to the much greater chance of swelling of the remaining parts in these animals. In the unilateral decerebrations in consequence the cavity has been merely filled with saline and it is conceivable that this might also be satisfactory even in the complete decerebrations. The other variations in the technique in the unilateral operation are described later (Chapter IV), since all these animals have been operated on by W. G. P. An attempt has also been made to get rid of the dead space in the animals by removing the whole cranial vault and drawing together the two temporal muscles over the base of the skull. Unfortunately it is not possible to make these muscles cover the space completely, nor is it possible to leave a smooth surface at the base of the skull without opening the nasal sinuses, and in our experience this had led to an infection of the wound with a regularity not seen in the paraffin method. For experiments lasting only three or four days, however, it is satisfactory.

The main difference between the later technique and the earlier one previously described is the horizontal section just above the level of the pituitary gland, allowing the blood-supply of this gland to remain intact. The contrast between the two methods may be seen by reference to figs. 9 and 10, which show photographs of a brain-stem operated on by the later method and comparing with them fig. 22, which illustrates the brain-stem left by the older technique. As in the earlier experiments the stalk of the gland was cut across, the blood-vessels supplying the anterior lobe must have been divided, and the gland itself may easily have been damaged and perhaps subjected to some pressure. In spite of this several animals survived for periods of two or three weeks, but as a rule they would not live more than three or four days. In these death was preceded usually by convulsive movements without signs of infection, or else was due to broncho-pneumonia. The convulsions occurring within three or four days were apparently similar to those described by Cushing [12] [13] as the result of removal of the pituitary, and consequently the modified operative technique was developed. This necessitates a more ragged incision with greater hæmorrhage, so that temporary control of the carotid arteries had to be also adopted. Following this change in the technique death on the third or fourth day preceded by convulsions has no longer been seen, and the animal's resistance to broncho-pneumonia has also seemed greater, but on the other hand, many more animals have been lost during the first day from reactionary hæmorrhage, and infection of the wound itself has also been more common.

The later technique has also given rise to some trouble, since the changed slope of the section has often been overdone, resulting in damage to the fifth nerve. Such damage must be avoided since it leads to the development of ophthalmia and pressure sores around the mouth, complicating the nursing and greatly increasing the risk of broncho-pneumonia.

(*b*) *Post-operative.*

The wound requires no covering, especially if it be stitched with waxed silk to prevent infection tracking inwards along the sutures, which may otherwise occur if the animal be kept in a bath. The wound may be left dry or covered with mercury ointment.

The main difficulty to be overcome is the maintenance of a constant temperature. For the most part the animals have been kept in a water bath, through which water was kept circulating and in which they were supported on a sling three-quarters immersed in the water. Stirrers maintained a constant mixing of the water, and a toluol regulator maintained the bath with a variation of only 0·2 to 0·4 C. in twenty-four hours at its best. Unfortunately, it often fell below this standard, as owing to post-war conditions the gas pressure sometimes fell so low as to be incapable of heating the large volume of water circulating through the bath.

In a bath the preparation readily gains heat from or loses heat to the circulating water, so that its rectal temperature rarely differs from that of the bath by more than 1° C. and practically never by more than 1·5° C. The bath has been usually kept at a temperature between 38° and 39·5° C. This method is possibly the simplest that will allow the maintenance of a constant body temperature in a preparation where the metabolism shows rapid variations, as it must in any which happen to show strong running reflexes. No ill effects from the prolonged immersion in water have been seen, even after two or three weeks, except a gradual shedding of the hair.

The disadvantages of the bath method are obvious, and it is this method that is mainly responsible for the paucity of our observations on the reflexes. Rough examination of the animal is possible as it is turned each day in the bath to avoid pressure sores, but in order to make any careful examination, it has to be taken out, washed in hot water, washed again with alcohol, roughly dried with a towel and finally dried in a hot incubator. Even with this technique, which requires four or five hours, the body temperature is apt to drop to 35° C. or lower, and though no ill results are noticed at the time, pneumonia often supervenes. Consequently any such examination will greatly decrease the preparation's chance of survival.

Owing to this many attempts have been made to keep them in an incubator. An ordinary incubator is useless, since the heat loss varies with the moisture in the air. Haldane [18] has shown the importance of the wet bulb temperature, but even an incubator controlled on a wet bulb basis is insufficient. The reason for this is that a very exact balance between heat loss and heat production has to be attained in these animals, and once this balance is upset the discrepancy tends to grow, since it is probable that in these preparations the metabolism falls with fall of body temperature instead of showing a compensatory increase. An incubator method has, however, proved possible by using an incubator heated by live steam escaping within it, so that heating occurs through condensation on its walls. In this way the wet and dry bulb temperatures are identical, the air being completely saturated with moisture. Even in such an incubator the control has to be altered during the first few days to match the gradual loss of the insulating action of the fur as it becomes penetrated with moisture, or this variation must be overcome by destroying these heat insulating properties of the fur by soaking the animal immediately after operation in petroleum oil. Under these conditions the animal loses heat mainly by radiation and conduction and usually keeps a rectal temperature about 4° C. above that of the incubator, so that this should be kept at about 34° or 35° C. The proper mixing of the air is ensured by an electrically driven fan. Further details of incubator experiments are given in Chapter III.

Food is given twice a day by stomach tube, a full-size cat requiring about 100 c.c. of milk at each feed. Great care must be taken to keep the mouth, eyes and nose clean, and the animal must be placed in a position which would be comfortable if it were conscious.

The chief causes of failure are infection, usually respiratory, less commonly infection of the wound, post-operative hæmorrhage, and in the earlier technique probably also pituitary insufficiency. No testicular atrophy nor adiposity has, however, been observed. One animal (previously reported) lost 10 per cent. of its weight in a week, but another (cat II) after twelve days "life" showed no change whatever in its body weight. Further experiments on the functioning of the pituitary in these animals are planned.

The prevalence of pneumonia in these preparations is of some interest in that it was commoner if the animals had been previously exposed to conditions giving them a low body temperature, even if this occurred a considerable time after their anæsthetization. An instance of this is seen in the case of cat II, which is described later.

CHAPTER III.—CHRONIC DECEREBRATE PREPARATIONS.

(a) *Details of Two Preparations.*

The characters shown by these animals can be best illustrated by recording a few examples in more or less detail and then giving a more general description. The question of the individual peculiarities in relation to the exact site of the section is a difficult one and will be considered later.

Animal I.—Young castrated male. Post-mortem examination, p. 239. 0·5 mgm. atropine subcutaneously after anæsthesia induced. Right carotid tied, left occluded temporarily. Trouble from hæmorrhage which was eventually stopped after using a cautery and leaving in muscle and cotton-wool plugs. Some cotton left in under wax. Section by the later technique with preservation of the vascular supply to the pituitary. Kept on a warm table for three hours it developed a hæmatoma from reactionary hæmorrhage during this time. Five hours after operation when in bath had moderate rigidity[1] and moderately brisk pinna reflexes. Bath temperature 39·4° C. Rectal temperature 39·8° C.

Second day. Conditions much the same. Good corneal reflex on left side but none on right.

Third day. Condition much the same. Respiration rate only 17.

Fourth day. All reflexes more sluggish. Rigidity still fair.

Fifth day. Reflexes as before. Rigidity stronger and fore paws kept extended and held rather backwards towards the tail. When turned on mattress slight kicking and extrusion of claws. Bath temperature 39·2° C. Rectal temperature 37·8° C.

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[1] Rigidity refers to the extensor rigidity of the limbs described in decerebrate preparations by Sherrington unless otherwise stated.

Seventh day. All reflexes more brisk. Rigidity fairly good. Respiration rate 19. Sores developing in mouth.

Ninth day. Pinna reflexes more brisk. Vigorous shaking of the head now present on blowing in the ear. Licking of lips and nose now present after feeding. Rigidity very variable, being either very good or else animal in flexed and fairly flaccid condition.

Eleventh day. Reflexes still improving. Rigidity almost absent in the morning but on turning the animal it became extremely marked. The limbs are moved somewhat if the pinna is twisted. If traction is exerted on the front paws there is a movement of retraction and flexion of the limb with extrusion of the claws.

Thirteenth day. Ophthalmia of the right eye now well advanced. Rupture of cornea. Condition as before, but when lying on left side has a position in which the fore limbs are rigid and extended (left more than right) and in which the left hind limb was also rigid and extended, but the right hind limb was rigid in a flexed position. Hind limbs now show retraction when pulled upon as well as the fore limbs, but there is no extrusion of claws in the hind limbs. If animal is stimulated by twisting the ear the head is raised, being bent either to the left or right according to which side it is lying on. No acoustic reflex present now or at any other time.

On fourteenth day as before. Crossed reflexes easily obtained in hind limbs. If right limb is forcibly flexed it stays flexed and then on pinching left limb the left is flexed and right extended and vice versa. On cleaning the left eye the animal moves its head, extending it dorsally as though objecting. General appearance of movement is that of a pseudaffective reflex.

Fifteenth day. Respiration rate 12 only.

Seventeenth day. Respiration rate 16. Reflexes much as before but very variable.

Eighteenth day. Found dead.

Animal II.—Female. Post-mortem examination, p. 247. Weight, 2·45 kilos. Old method used and the cranial cavity scraped clean to the tentorium. Kept in incubator for one hour and then put into bath. Eight hours later fed, 100 c.c. of milk. Rigidity then good and pinna reflexes and corneal reflexes brisk. On following day these reflexes still brisk, respiration rate 20, bath temperature 39·2° C., rectal temperature 38·1° C.

After two days reflexes more brisk. Acoustic reflex now present; animal shakes its head slightly in response to loud noises.

Fourth day. Reflexes not quite so brisk; rigidity still good.

Fifth day. Vomited after the morning feed.

Sixth day. Reflexes much more brisk and rigidity very good. When lying on right side moves head slightly when hands are clapped; with high note of a whistle lifts head up from the rest, bending it to the left. When lying on left side acoustic reflex scarcely noticeable, since the head is pressed downwards to the left.

Seventh day. Reflexes much more brisk, especially acoustic. If lying on right side now lifts head well up when anyone walks into the room, unless on tiptoe. Very brisk response to slight scratching noises. Pushes head downwards as before in response to sounds if lying on the other side.

Eighth day. Bath outlet choked. Animal taken out and dried during cleaning of the bath. During the drying, temperature fell to about 34° C. and remained subnormal about two hours. Weight when dry 2·4 kilos. Rigidity fairly good but not so strong as previously, and animal does not remain well in a sitting position as do most preparations. Acoustic reflex confined to head and neck movements. On touching the animal running movements are developed with strong movements of the front limbs and only slight in the hind limbs. Returned to the bath after eight hours.

Ninth day. Keeps eyes open, though previously they have been kept shut. On whichever side it is lying the upper fore limb is held passing forwards and downwards across the other, the lower fore limb passing somewhat backwards and upwards. This position is a very characteristic one and is seen in a large percentage of the preparations.

Eleventh day. When lying on left side responded to stimulations such as twisting of the ear, by kicking and some slight movement of the head. Rigidity intermittent and less marked than before.

Twelfth day. When being turned on the mattress kicks vigorously. Taken out of the bath in the evening and dried preparatory to Physiological Society meeting at Oxford. During drying temperature fell to 36° C. and remained subnormal for several hours.

Thirteenth day. Weight when dry 2·45 kilos. Respiration rate 24. Reflexes very brisk as before and kicking movements when the animal is stimulated. During most of the time the animal did not have a typical extensor position but remained moderately rigid in a semi-flexed posture and with a rigid flexion of the ankle-joints of the fore limbs. Temperature fell again to 36° C. during the afternoon when exhibited at the Physiological Society. Replaced in bath in the evening. Animal had sores from friction under armpits and during replacing in the bath made inco-ordinated attempts to reach the sores with its head and hind limbs.

Fourteenth day. Respiration faster. Animal kicking a lot when touched.

Fifteenth day. Respiration 66. Reflexes very poor.

Sixteenth day. Respiration 44. Reflexes slightly better.

Seventeenth day. Respiration 32. Reflexes good, except for acoustic, which has been absent since the fourteenth day.

Twentieth day. Respiration 24. Acoustic reflex present again for the first time since pneumonia began. Fore limbs rigid, extended and without movements. Hind limbs have a curious slight walking movement even when animal is not touched.

Twenty-first day. Kicking movements when stimulated. Made occasionally a curious sound like an inco-ordinated mew.

Twenty-second day. Respiration 22. Pinna and corneal reflexes very brisk. Acoustic reflex good. Touching the face produces twitching of facial muscles, and even a slight movement of air across the face produces the twitching of muscles and shaking of the head. If animal is stimulated by twisting the ear curious walking movements occur, most marked in hind limbs, and sometimes accompanied by a curious crying sound.

Twenty-third day. Had caught fore-paw in thermo-regulator and had broken it. Animal found dead and temperature of bath 41° C. Death no doubt due to hyperpyrexia.

These two examples give a fairly good general impression of the results usually obtained, though there can be no doubt that the first of these showed some symptoms of raised intracranial pressure secondary to hæmorrhage and infection throughout its time of survival; it is probable that raised intracranial pressure caused absence of function of nervous centres close to the section, thus accounting for the sluggish reflexes and the relative simplicity of the reactions in the late stages compared with those shown by many animals.

(*b*) *Posture.*

The decerebrate rigidity remains as a general rule during the whole time the preparation survives, but after the first four or five days this position is less constant, and may alternate with others in which flexion, either flaccid or rigid, is conspicuous. At this later stage the variability of the positions assumed is noticeable, and it seems probable that the temporary disappearance of the rigidity is due to the assumption of other reflex positions. The maintenance of good rigidity over a long period, as in animal I, certainly makes it possible to exclude it being due to stimulation of cut nerve fibres, since these had undergone degeneration in this animal, and there is, therefore, good confirmation of the generally accepted view of the reflex origin of this position.

The rigidity shows variations according to the position of the animal, and to some extent these variations correspond with those described by Magnus and Kleijn and their co-workers [3], [26], [27], [28], [36], [37], [38], [39], [40], [61], but in the few animals that we have examined carefully we have been unable to get such consistent results as these authors have described. As in our animals the spinal cord has not been divided, the rigidity of the fore limbs is influenced by the position of the hind limbs, so that less constancy must be expected. In general with the animal lying on one side all four limbs are held rigidly extended, but both the upper fore and hind limbs are relatively flaccid when compared with the lower. This difference is still observed if the animal is suspended in the air by holding it up by its skin while maintaining it in a similar position, but the difference in rigidity is less noticeable than it is when the animal is also receiving pressure stimuli by resting on the table. This contrast between the upper limbs and those resting on the table was very constant and was noticed in a large percentage of the animals, but even in this respect preparations are found in which this difference is scarcely noticeable, or in which the rigidity is asymmetrical so that the contrast cannot be observed. This asymmetry is especially apt to occur in the later stages when a position of general extension of the limbs is much less constant.

During the first few days the position usually assumed by a preparation lying on its side is that described already in the case of animal II on the ninth day, the position of the hind limbs being variable, though most commonly the upper hind limb was also held rather forwards and the lower farther back. On turning the animal over the limbs move, so that the same posture is assumed in the new position. This again is not regular; thus, for instance, in one of the earliest of these experiments, an animal (decerebrated June, 1914) maintained this posture constantly on whichever side it was lying, except on the second and seventh (the last) days, when the relative position of the limbs was the reverse of this, the lower fore limb being held forwards and the upper fore limb backwards. That this was a definite posture was demonstrated on turning the animal; then the limbs were moved so that this atypical posture was adopted also when lying on the other side. Such an atypical posture has sometimes been maintained by other preparations and has then been the usual position for that animal.

Rigid flexed positions may be assumed in an acute preparation, but under these conditions it is rare, and we have never been able to produce them, except accidentally; in the chronic preparations they are a comparatively common occurrence, and indeed some degree of flexion is usually found in one or more of the limbs after the first five to ten days, and, though it may alternate with extension, yet flexion may sometimes be the more constantly maintained posture. The most common of these flexed positions is a rigid semi-flexion of the fore limbs, or of one fore limb, with an acute rigid flexion of the ankle joints and extrusion of the claws of the fore limbs. The position is then one similar to that assumed by a cat when holding a mouse in its claws or when climbing up a pole. An example of this will be seen in the case of animal VIII, of which a detailed description will be given later. A few other instances may be brought forward.

Animal III.—Large male. After operation had rigidity of average intensity present in all four limbs; the rigidity was fairly symmetrical, though the head was held turned to the left. On the third day this rigidity became less noticeable and when turned the animal tended to curl up and flex the fore limbs. On the fourth day after turning, the previous degree of rigidity had returned, and was maintained on the fifth day. On the sixth day there was a rigid flexion of the ankle joint of the upper fore limb, on whichever side it was lying, with extrusion of the claws of this limb. On introducing a thermometer into the rectum both fore limbs were flexed with acute flexion of both ankle joints and extrusion of the claws, while several extensor thrusts were made with the hind limbs. In this animal the section passed through the anterior end of the right superior colliculus and through the middle of the left superior colliculus, to emerge ventrally 3 mm. in front of the pons at the level of the stalk of the pituitary, but no microscopical examination was made. This animal also gave pseudaffective reflexes and will be referred to again later in this connection; the decerebration was by the older method in which all the brain above the section was removed so that there was no possibility of any connection with higher centres.

Animal IV.—Adult female. Post-mortem, see p. 250. Decerebrated by the later method, the rigidity was only moderate on the first day, but increased on the second, though still below the average; on the third day the animal kicked a good deal during turning, and then assumed a position of rigid flexion of the back and hind limbs with some flexion of fore limbs. On the fourth day there was an average rigidity in an extensor position, but flexion postures were assumed temporarily, during turning, &c., but were maintained only a few minutes, then gradually changing to an extensor posture. On the sixth day the animal was taken out and dried for examination in greater detail. On taking it out of the bath it went into a position of extreme extensor rigidity with retraction of the head. During drying with a towel it made many movements, kicking, withdrawing a limb that was being dried and shaking it, especially the left hind limb. It also made some progression movements. In between these movements positions either of rigid flexion or of rigid extension were assumed.

In the rigid flexed position the ankle joints of the fore limbs were acutely flexed and the claws extended. Unfortunately this animal vomited and choked during drying, so that no further examination was possible.

A position of flaccid flexion was also not uncommon in the later stages. An instance of this is described below.

Animal V.—Half-grown male. Post-mortem, see p. 250. Decerebrated by the later method. Three hours after operation showed little rigidity but made walking movements most of the time. For the first nine hours the animal was kept in an incubator but developed little rigidity; it was then put into a bath and on the next day the limbs had good extensor tone. On the third day there was little or no rigidity. On the fourth day rigidity was absent in the morning, the limbs being quite flaccid, but quite good rigidity developed on turning it to the other side. On the fifth day the rigidity was moderate and on the sixth it had again disappeared, though the pinna and other reflexes were good. The animal was then dried. On washing in alcohol and drying with a towel there were good movements of retraction with a shake of the paw of the limb being dried, especially in the fore limbs, and good extensor rigidity returned temporarily. When dry the animal appeared completely flaccid, with good pinna reflexes, shaking of the head on blowing in the ear, and retraction and shake of each limb on pinching. It was then given to Professor Sherrington for use in his experiments. As soon as dissection was started, kicking movements of all four limbs with movements of the head and neck were made, the animal micturated and then the preparation went into a posture of extreme extensor rigidity with considerable retraction of the head which it then maintained. Following this the extension became gradually less intense, though never disappearing entirely within at any rate twenty minutes, and was renewed in full intensity as soon as the preparation received further stimulation.

Other preparations were sometimes flexed and perhaps flaccid as they lay in the bath, but went into extensor rigidity immediately any examination was attempted. In one or two cases this passage from a flexed to an extended posture seemed to be induced by mere auditory stimuli, but no instance of this was seen in which the evidence was absolutely conclusive, owing to the difficulty of observing the animals while in a bath. It is conceivable that the flaccid flexion is a posture which has some relationship to the sleeping of a normal animal, but no proof of this is available.

Of the animals so far described two (animals II and III) have been distinguished by a tendency to turn their head to the left. This was a common occurrence, being noticed in fourteen animals as compared with nine that turned their heads to the right. This may have been due to the fact that the trephine opening was made on the left side and in consequence the section was generally a little oblique, and nearly always with the tendency to the removal of more on the left side. In thirteen of the above fourteen cases with head held to the left more brain matter was removed on the left side than on the right. On the other hand, of the nine preparations (see cats VI, VIII, XV, XXII, XXIV), in which the head was held turned to the right, in four the section appeared to be evenly transverse, in four the section had the usual obliquity (more being removed on the left), but the turning of the head to the right was observed in spite of this; the level of the section was not determined in the ninth. The relationship is evidently complex, since the section had the usual obliquity in other cases without there being any asymmetry in the head position; undoubtedly during the first few hours stimulation may play a part.

In the one animal with more brain-stem removed on the right, which turned its head to the left, the position assumed may well have been due to stimulation, since it occurred during the first day, after which the animal died. Stimulation immediately after operation would also account for three out of the four cases in which turning the head to the right was noticed, although the section had removed more brain on the left side, since in these again the turning of the head was only noticed during the first day. In the animals with an apparently square section, in which the head was turned to the right, this posture was not marked except in one case. In all cases where there was an asymmetrical head position the level of the section was relatively anterior, and some few cells of the red nucleus were probably left intact and may have been functioning on one side at least. In fact, this whole turning of the head to the side most damaged might be explained if the tone of the muscles of the neck was increased by a crossed connection with a centre lying at about the level of the section, and it is possible that the lowermost cells of the red nucleus may function in this way.

Of the thirteen animals showing a persistent turning of the head to the left, one (XXVI) has been shown histologically to have had more of the red nucleus remaining on the right side than on the left, and in all the others the section was sufficiently high for a part of the red nucleus to remain, with the possible exception of two. The most difficult case to explain is that of animal VI (for post-mortem see p. 249) in which histological examination showed an almost complete destruction of the left red nucleus, the right red nucleus being partly present though showing some chromatolysis. Yet this animal gave auditory reflexes with movement of the head to the right during the two days it survived. Unless the hæmorrhage had interfered with the tract from the right red nucleus, the above hypothesis would seem untenable, and it cannot be regarded as established at present; further the posture is not easily correlated with results of stimulation of the mid-brain reported by Graham Brown [8].

Many of the animals had sufficient rigidity to stand if propped into position, as described by Sherrington in the acute preparation, and most of them were able to maintain a very natural sitting posture. This consisted in making the animal lie on one side and propping up the body on the two elbows, so that the head was held in an erect position. Many could sit in this position on either side and maintain it for a considerable time, though usually after about five minutes the head would gradually drop, being allowed to fall sideways, and the preparation would lie down, the head in this procedure being carefully lowered so that no sudden impact with the table occurred. Similarly, the head was gently lowered if the animal was pushed over out of its sitting position. If the animal spontaneously held its head to one side, it was often only possible for it to balance itself in this sitting posture when lying on the flank opposite to the side to which the head was turned. All the postures assumed are more or less comparable with some seen in normal cats, the flexed positions that are often assumed in the later stages resembling those of cats curled up asleep.

(c) *Magnus Reflexes.*

These have been carefully investigated in two animals only owing to the difficulties with animals kept in a bath, though a few data resembling his results have been obtained on one or two other animals,

Animal VII.—Male, three-quarters grown. Post-mortem, see p. 251. Decerebrated by the later method. On examination twenty-seven hours after operation the animal could sit on either side and had good rigidity of all four limbs when standing, sitting, or lying on its right side. The rigidity of the fore limbs was less than that of the hind and was almost completely absent when the animal lay on its left side. In the standing position little change in rigidity was noticed as the result of raising or lowering head, and when lying on its back there was scarcely any rigidity in the fore limbs in any position of the head. When lying on right side bending the head down to the right increased the tone in the two hind limbs, and rotation of the head (jaw upwards) caused increased tone in the left fore and hind limbs and a slight decrease in the right hind limb, with no perceptible change in the right fore; the opposite changes occurred on turning or rotating the head in the opposite direction. Lying on the left side bending the head up to the right increased the tone in the right hind, but no other change was distinguishable, and rotation (jaw upwards) also increased the tone in the right hind, slightly increased that in the right fore, and slightly decreased that in the left hind; the opposite effects were obtained by the reverse movements.

Animal VIII.—Female. Post-mortem examination, see p. 252, and for more detailed description of the animal see p. 208. Decerebrated by the later method. Examined on the seventh day. When lying on its back reflexes orthodox, showing flexion of the fore-limbs when the head was bent right forward, maximum rigidity with head in −45° or +30° position, this decreasing a little as the head was moved to 0°. This animal had little rigidity in the standing position and could not be made to stand. Placed on one side it assumed always a definite posture on whichever side it was lying; in this the lower fore was completely extended, the lower hind three-quarters extended, the upper hind semi-flexed and the upper fore was flexed and carried forward over the other, and the position of all the limbs was a rigid one. On flexion of the terminal joint of the upper fore there was extrusion of the claws. While lying on the left side bending head to the right caused extension of all limbs except that no change was noticed in the right fore; when on the right side there was extension of both fore-limbs and slight flexion of both hind on bending the head to the left. Lying on the left side, rotation of the jaw upwards caused extension of both hind-limbs and no perceptible change in the fore-limbs; on the right side rotation of the jaw upwards caused flexion of left hind and right fore, and extension of left fore, but no change in right hind. Movements of the head in the opposite directions in every case reversed the changes in the limbs, with the exception that rotating the head (jaw downwards) when the animal was lying on its right side not only reversed the changes in rigidity described for the opposite movement, but also caused a movement forward of the left fore-limb. In this cat the rigidity was slightly asymmetrical, since the preparation could sit on either side, but did so more evenly and securely if resting on its left flank, and it showed some tendency for the head to turn to the right. Some such asymmetry may account for the atypical reactions to these tests. The preparation died soon after the examination, apparently owing to a secondary hæmorrhage at the base of the brain.

(*d*) *Opisthotonos.*

This is not uncommon immediately after operation; in these animals the respiration rate is usually slow (though sometimes there is a fast and shallow respiration), and the condition is generally accompanied by tonic fits in which the rigidity undergoes extreme accentuation. In fact this head position was never seen except accompanying extreme extensor rigidity and merely appeared to be the result of such extreme rigidity. A few instances may be described.

Animal IX.—Old male. Post-mortem, see p. 247. Decerebrated (earlier method) 3.30 to 4.30 p.m. At 5.30 p.m. put into bath. Extreme rigidity, especially of hind-limbs.

Head retraction but not extreme. On second day reflexes brisk. Extreme rigidity of all four limbs. Lifts head to left to acoustic stimuli, but no opisthotonos now seen. On ninth day extensor rigidity still good, having remained very marked since operation, but auditory reflex has almost disappeared since fifth day. Head retraction now again present. The rigidity of the hind-limbs is, however, definitely less than before, the fore-limbs are fairly rigidly extended except for a rigid flexion of the ankle joint with extension of the claws like that described in cat II. In the evening showed marked rigidity of mastication muscles with some clonus of the jaw on opening the mouth. Some nystagmus of eyes with rapid movement to the right, especially seen in the right eye. On the eleventh day found dead, and evidence found of old hæmatoma with later infection.

Animal X.—Decerebration (earlier method) 2.45 to 4.15 p.m. Considerable hæmorrhage. At 9 p.m. in incubator, rectal temperature 41·2°, respiration rate 24, rather irregular, and each inspiration accompanied by slight spasm of muscles of back. Rigidity intense and whenever the animal is touched it goes into extreme opisthotonos. At 10.45 p.m., temperature 38·8°, respiration rate still 24, with long inspiratory pause and only occasional spasm of back muscles. Attacks of opisthotonos as before. This opisthotonos was brought on most easily by touching the nose; it could be made to relax generally, but not always, by flexing the head, and would itself relax spontaneously to some extent after a time. On one occasion insertion of a thermometer into the rectum produced a strong defæcation reflex with immediate relaxation of the intense rigidity and disappearance of the opisthotonos.

On the following morning the opisthotonos had disappeared, breathing was more regular, 20 per minute, with a rectal temperature of 37·8°. Rigidity marked but not so intense, and twitching movements of all four paws present, these occurring with each inspiratory movement. On the third day respiration normal, muscle spasms no longer seen, and the animal made an inco-ordinated mew twice when taken out of the incubator. Animal died at the end of the day and post-mortem showed a considerable hæmatoma at the base of the skull. No detailed examination of the level of the section.

Animal XI.—Female, half-grown kitten. Decerebration (later method) 2.30 to 3.15 p.m. Signs of reactionary hæmorrhage immediately after operation with considerable oozing from the wound. Attacks of marked rigidity and head retraction. Found dead next morning. On autopsy considerable hæmatoma; the section extended from in front of superior colliculi to about 0·5 millimetres behind the anterior end of the pons.

It will be clear from these examples that this condition is seen in animals with evidence of post-operative hæmorrhage, and generally blood is also found below the tentorium. Death in the first twenty-four hours is common, but if the animal survives the opisthotonos disappears, and does not reappear again except in the case of an infection of the base of the skull such as was the case in animal IX. The exaggeration of the position as the result of some sensory stimuli, and its inhibition by other stimuli, is also another noticeable feature. In some animals auditory stimuli or a jar such as that from shutting the incubator door seems to have been sufficient to induce a head retraction spasm.

Head retraction of less intensity may occur in animals with a normal degree of rigidity if this be exaggerated temporarily by nervous stimuli such as the dissection of a nerve. An example of this was seen in animal V, which has already been described. Reflex factors, as well as conditions with raised intracranial tension, must therefore also play an important part, and this condition is merely an exaggerated extensor rigidity.

While a hæmatoma and usually subtentorial hæmorrhage have been found in all such cases, many other animals may show quite similar hæmorrhage on autopsy and yet have never presented these symptoms. The cause of opisthotonos cannot be hæmorrhage into the fourth ventricle, since it has been observed in animals in which no such hæmorrhage was found.

(*e*) *Temperature Regulation.*

There seems to be no doubt that after operation these preparations have no power of temperature control whatever, and that they never regain it however long they may survive the operation. If they are kept in an incubator the setting of the incubator temperature has to be exactly right, so that the heat loss balances the heat production, in order to maintain a constant temperature, and the setting of the incubator required for different animals is not the same. Even for the same animal the balance has to be hit exactly, taking into account the degree of the dryness or dampness of the fur, and to strike such a balance becomes a difficult problem even if the air be maintained saturated with moisture.

Not only are they unable to adapt themselves to even small changes in temperature but they have never shown normal reactions to these temperature changes. If their body temperature is dropped suddenly no shivering has ever been observed, nor does their respiratory rate increase to a normal extent if their body temperature is quickly raised. It is true that few people have seen a normal cat shiver in cold weather or pant under the influence of heat, but anyone who has tried washing a cat will have observed the shiver (see also animal V), and if a wet cat be dried under sufficiently warm conditions the respiratory rate may easily rise to 70 or 80 a minute. The ordinary cat does not usually show either symptom, since it is careful to keep itself under comfortable conditions and has a thorough insulation in its fur. The metabolism of these preparations has not so far been investigated by us, but we have no reason to doubt the low metabolism figures obtained on the acute preparation by Roaf [47], since the difficulty of keeping the preparations warm has always been remarkable. The stretching out of the limbs in extension no doubt increases the heat loss, but even so it is surprising that keeping the animals on a warmed operation table, surrounding them with hot-water bottles and covering with a blanket, is usually only just able to keep the animal's temperature normal if the room is at all cold, i.e., 15° C. There is also some evidence that the metabolism is greater the higher the temperature and that it decreases with a fall in temperature, so that there is no effort at a control of body temperature through a control of metabolism. Thus in an incubator animal with its fur greased and in an atmosphere saturated with moisture (when the loss of heat is accomplished by radiation and conduction), the difference in temperature between the animal and the incubator is usually greater the higher the temperatures happen to be. Thus with a high rectal temperature a difference of 5° C. above the temperature of the incubator may be found, and with a low rectal temperature the difference between the two may be only 3° C. Thus there is a tendency for the rectal temperature to swing more widely than that of the incubator. The resulting difficulty in finding a correct setting for the incubator is readily seen by reference to a few examples.

The general correspondence between the animal's temperature and that of the incubator is well shown in fig. 1, which represents the temperatures observed in cat VII, of which some description has already been given. This animal was kept immediately after operation in an incubator in which the air was constantly saturated with moisture by having the wall covered with damped cloth. Considerable difficulty was found in getting a correct setting of the incubator and it is seen that between eight hours and twelve and a half hours on the first day the rectal temperature of the preparation dropped 2·1° C. (from 37·2° to 35·1° C.), corresponding with a fall of 1·5° C. in that of the incubator. It is also noticeable that after three and a half hours on the first afternoon the rectal temperature was 39° C. and was rising rapidly as the result of an incubator temperature of 29·7° C. dry and 29° C. wet bulb, while twenty-seven hours after operation the rectal temperature was fairly steady at only 36·2° C., though the incubator setting had now been adjusted to give a temperature of 30·3° C. dry and 29·8° C. wet bulb. The difference in the two results is probably due to the gradual loss of the insulating action of the fur as the effect of the penetration of the moisture through it. This was demonstrated accidentally on the second afternoon. At 3.10 p.m. the animal was taken out of the incubator and was examined for Magnus reflexes in front of a gas stove until 4.25 p.m. During this examination its rectal temperature rose to 39·7° C., its fur became dry and in good condition, and it was then returned to the incubator in the belief that its temperature would gradually drop again to 36·2° C., since the incubator setting had not been altered. The observer was interrupted by teaching work and when the animal was again examined, one hour and thirty-five minutes later, it was found to be dead, with a post-mortem rectal temperature of 42·1° C. This case, therefore, illustrates very well the difficulties of incubator preservation of these preparations, and the numerous factors that have to be taken into consideration, as well as demonstrating the absence of any control.

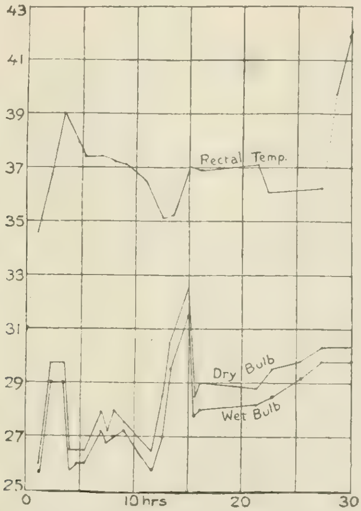

FIG. 1.—Experiment VII. Abscissa: Time in hours from end of operation. Ordinate: Temperature degrees centigrade. Lowest curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Upper curve: Rectal temperature of animal. Dotted part of curve: Change when animal was out of incubator being examined in front of a gas stove.

The same points, and also the general course of such an incubator experiment, may be seen in the case of cat VIII (also previously described in relation to the Magnus reflexes). The general history of its temperature changes is illustrated in fig. 2; but a more or less detailed account may also be given to serve as an example of an incubator experiment.

Animal VIII.—Female. (For post-mortem see p. 252, and previous description p. 203). Decerebrated by later method so as to preserve stalk of pituitary. Rather ragged section and considerable hæmorrhage afterwards. Large piece of gauze left in, but in spite of this a considerable hæmatoma formed shortly after the end of the operation. Placed in steam-heated incubator at 30·8° dry and 30° C. wet, i.e., about temperature at which cat VII had a rapid rise of temperature on its first day. At three and a quarter hours the rectal temperature was still below 35° C.; at four and a quarter hours it was still only 34° C., though the incubator temperature had been still further raised. The incubator was then set to give 33·5° dry and 32·8° wet bulb, and the rectal temperature gradually rose to reach 38° C. after about nine hours. The incubator temperature was then gradually reduced and regulated to give a temperature of about 31·5° dry and 30·5° wet bulb, when the rectal temperature reached a steady level at about 37·3° C. During this time the animal had had good rigidity of all limbs; twelve hours after operation it showed brisk corneal and pinna reflexes, and some mastication reflex, and when the ear was twisted it moved its head and fore limbs slightly and showed a definite increase in decerebrate rigidity.

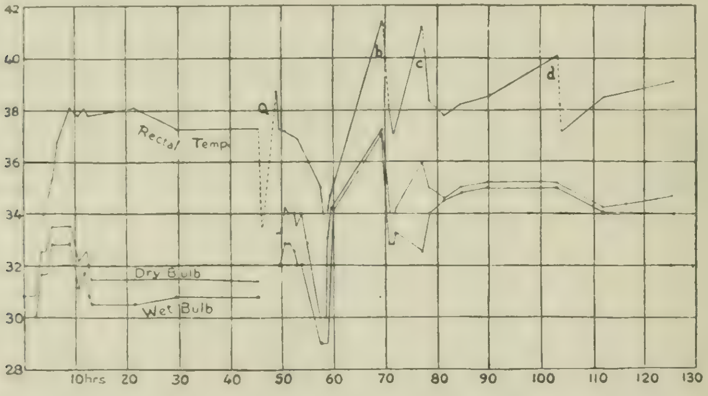

FIG. 2.—Experiment VIII. Abscissa: Time in hours from end of operation. Ordinate: Temperature. Lowest curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Top curve: Rectal temperature of animal. Dotted parts of curve: Animal out of incubator—(*a*) taken out, wound dressed; as bodily temperature fell fur treated with paraffin and animal then warmed in front of gas stove; (*b*) and (*c*) cooled by being kept in a room for a short while; (*d*) examined in front of stove for Magnus reflexes.

Thirty hours after operation reflexes as before but mastication no longer seen; respiration rate 21, temperature 37·3° C. Lying on right side it now had good rigidity of all four limbs, but on turning on to left side showed some flexion of back, good rigidity of hind limbs, little rigidity in the left fore, and it held the right fore rigid, but flexed and placed forward across the left, with the ankle joint acutely flexed and the claws extended. It kept its head turned to the right if put into a sitting posture. The tail was intensely rigid, and was wagged whenever the animal was touched.

Forty-six hours after operation taken out of incubator, and gauze plug removed from wound; hæmatoma found infected. Animal kept on warmed table but room temperature only 9° C. (owing to post-war conditions), and the rectal temperature soon dropped to below 35° C. Animal then warmed in front of gas stove and lubricating oil rubbed into fur to diminish its heat insulation value.

Returned to incubator at 2 p.m. (i.e., fifty hours after operation) with temperature of 38·7° C. The respiration rate was then 20, having dropped to 15 per minute when the body temperature was at its lowest. Fig. 2 shows the changes in temperature occurring after this and the close correspondence between the rectal and incubator temperatures. When the rectal temperature had risen to 41·6° C. the respiratory rate was 40, dropping again to a rate of 31 when the rectal temperature had reached 38·1° C. on taking the animal out of the incubator and keeping in a cold room. This drop of temperature occurred in about thirty-eight minutes, and yet there was never any sign of shivering. The posture of the animal when lying on the left and right sides was as before. The wound was opened up and some pus evacuated.

Sixty-six hours after operation the animal was again examined. It now had good extensor rigidity of all four limbs when lying on the *left* side, and on being turned to the *right* side there was good rigidity of the hind limbs and extrusion of claws, and on stimulating by twisting the ear the fore limbs assumed a rigid flexed position with extrusion of the claws, and maintained it.

One hundred and three hours after operation the rectal temperature was 38·5° C., and the respiratory rate 32. The upper fore limb was kept flexed on whichever side it was lying. On touching the animal there was reflex extrusion of claws and either retraction or prodding forward of the limbs.

One hundred and eighteen hours after operation the animal was much as above, but when traction was made on its flexed upper fore limb, it withdrew it with a clawing movement. It also made a cry—an inco-ordinated mew—when being turned.

One hundred and twenty-seven hours after operation was as above but on various stimuli, such as mere touching, would often extend a limb and spread out claws, in the position a cat holds its limbs when stretching after waking up.

At the end of the sixth day the position of the animal on whichever side it was lying was very definite and has already been described in connection with the Magnus reflexes. It had no auditory reflexes, but by this time some mastication had again returned. The respiration rate was 33 with a rectal temperature of 39·1° C. There was a discharge of pus and wax with disintegrating hæmatoma from the wound, and in the middle of the seventh day the animal died as the result of a secondary hæmorrhage within the cranium. Urine passed during the third day contained no trace of sugar.

The effect of body temperature on the respiratory rate is also well shown in the case of cat XII kept in an incubator with a wet bulb control, but in which the air was not saturated with moisture and where the insulating action of the fur was not interfered with. The changes in body temperature and of the incubator for thirty hours, starting seven hours after the end of the operation, are shown in fig. 3; the wet and dry bulb readings were taken at frequent intervals and the rectal temperatures were taken with an electrical resistance thermometer and were recorded every minute on a Gamgee [16] thread recorder as described by Woodhead and Varrier Jones [65]. In all, more than forty-five observations of the respiratory rate at varying body temperatures were made on this animal, though the results were somewhat modified by the gradual development of mucus in the trachea giving some irregularity in the respiration with a later development of lung congestion. If all the figures for the respiratory rate during the first few days are averaged the following results are obtained:—

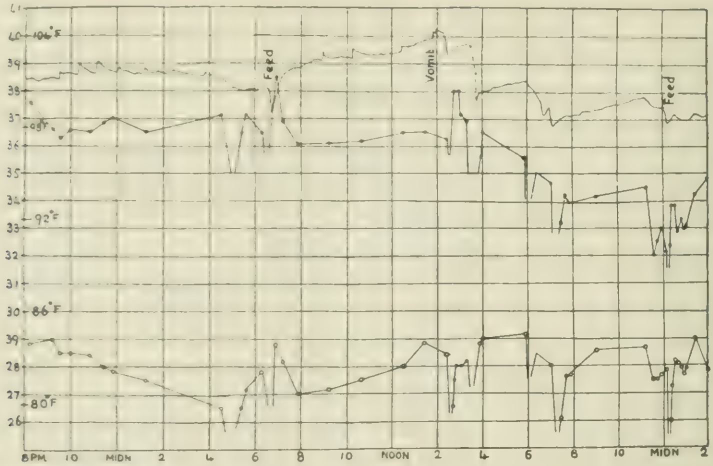

Fig. 3.—Experiment XII. Abscissa: Time: operation finished seven hours previous to commencement of record. Ordinate: Temperature. Lower curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Upper curve: Rectal temperature of animal (record with resistance thermometer). Gaps in records, opening of incubator door.

Temperature	Number of observations	Average rate per minute
36°.1 to 37°	4	23
37° to 38°	18	28
38° to 39°	16	33
39° to 40·1°	7	36

If, however, only the earlier figures are taken, before much tracheitis had occurred, the respiratory rates are rather slower but the relative differences are much the same.

Average temperature	Number of observations	Average rate per minute
36·1°	1	15
37·2°	4	19
37·8°	5	25
38·0°	2	29
38·3°	4	31
38·7°	4	32
39·5°	3	33

The brain section in this animal was from the anterior end of the inferior colliculi to 1 mm. in front of the pons, but a detailed histological examination was not made. It will be noticed that in this animal as well as in cat VII there was a very definite dependence of the respiratory rate on the body temperature. This is still more clearly seen in fig. 4 in which the respiratory rate observations are plotted against the body temperatures. The figures are obviously affected by other factors, such as the mucus already referred to, and quite possibly the respiratory rate is different for any given temperature, if the temperature is then falling, compared to what it would be if the temperature were rising. In spite of these variable factors it is clear from a consideration of these two examples that there is a relationship, and that the temperature coefficient is rather high, probably about 4·0, possibly as high as 5. But in any case the effect is much less than in the normal cat where a slight rise in body temperature may easily

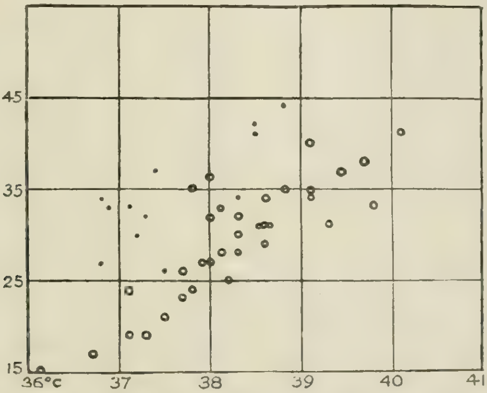

FIG. 4.—Experiment XII. Abscissa : Rectal temperature. Ordinate : Respiratory rate per minute. Variations in respiratory rate with changes in temperature. o = Observations during first twenty-nine hours. . = Observations made later than this.

give a respiratory rate of 80 [20] [30] [48]. That the temperature coefficient is so high may be partly due to the fact that not only might the change in temperature affect the respiratory centre directly, but it might also do so indirectly through altering the metabolism.

In only one instance was a really fast respiration seen with a raised body temperature. In this animal the temperature rose to 42·8° C. in an incubator through an accident. At the time of observation it was moribund and its respiratory rate was about 60, but this animal had had a considerable reactionary hæmorrhage, with marked opisthotonos and convulsive spasms, and its fast respiratory rate may have been due to other factors. In any case the rate observed is not very different from what might be expected at this body temperature, judging by the other animals. The section in this animal was also rather anterior and very ragged.

With regard to the respiration it should be noted that as a rule with a normal body temperature the respiratory rate was about 24 per minute, which is about the normal rate for a cat. Irregular and spasmodic breathing described by Macleod [34] [35] as occurring spontaneously in some animals after decerebration was not seen except where there was fairly definite evidence of hæmorrhage, as in cat X, nor can we agree with the provisional statement made by Macleod that "when the posterior corpora quadrigemina are even slightly wounded spontaneous respiration is seldom, if ever, observed." We have repeatedly made sections through this level and observed normal respirations, and we have even made sections through the very posterior edge of the inferior colliculi without having trouble with the respiration (e.g., cat XXI described later, survived over twenty-two days with a normal respiratory rate, and cats XX and XXIII furnished other examples of this). The contrast between our experience and that of Dr. Macleod may depend on the fact that our animals immediately after the operation were left quite quiet without further experimentation, while such a course is impossible in dealing with the acute preparation. Any manipulation or stimulus must increase the risk of reactionary hæmorrhage either below the tentorium or into the substance of the medulla, and that this was a common occurrence even in our animals may be seen by reference to the anatomical descriptions. Clearly the macroscopical inspection of the brain-stem does not allow the physiological level of the decerebration to be determined, and consequently discrepancies between different observers are to be expected according to the relative probability of post-operative hæmorrhage. A similar explanation may well account for the discrepancies between Trevan [58] and ourselves as to the effect on the respiratory rate of section at various levels.

Fig. 3 demonstrates well how sensitive the body temperature was to the changes in the incubator produced by opening the door for a few minutes, as for instance for feeding.

That the wet bulb temperature is very important is shown by the fact that animal VII required a wet bulb temperature of about 29° C. with a dry bulb reading of about 30° to maintain a normal temperature, while animal XII required a wet bulb temperature of between 28° and 29° with a dry bulb of about 34° for the same result. And yet it was not the only factor; the rectal temperature showed a rise in cat XII between 8 a.m. and 2 p.m. with a rise in the wet bulb temperature, but it also showed a fall between 4 p.m. and 10 p.m. although the incubator wet bulb temperature had altered very little, while the dry bulb fell considerably. Also the difference seen between animals VII and VIII, one requiring a wet bulb temperature of 29° and the other of 31° (before the fur was greased) with almost complete saturation with moisture, to maintain normal conditions, requires explanation. Cat VII had an excellent coat and cat VIII was rather mangy, and this may well have been the cause.

The incubator temperatures in the case of cat XII were rather variable; the reason for this was that the outer door of the incubator was left open throughout the experiment to allow the repeated examinations of the respiratory rate on this animal, and the glass door did not give adequate insulation. The sudden peaks occurring in the rectal temperature record in this figure are also of interest. They were always seen when an animal attempted to defæcate against the resistance of the thermometer; since they show fairly steep falls directly the efforts ceased they may represent a change in temperature which was chiefly local.

The absence of shivering on cooling was specially tested in one animal (cat XIII) four hours after operation. This animal's reflexes were brisk and the section was an anterior one passing through the superior colliculi to 2 mm. in front of the pons; it was operated on by the older method. Though its temperature was reduced from 39·5° to 37·8° by wetting with cold water (the normal temperature for a cat is about 38·5°) within five minutes, yet no sign of shivering was seen. In another animal which has already been referred to (cat V) the preparation was kept in an incubator for the first nine hours; it was constantly making running movements, so that it was not found easy to balance the heat exchange. At the end of this nine-hour period its rectal temperature was 40·9° C.; then it was cooled down by holding under a tap delivering water at 16·5° C., the water being rubbed into the flanks, so that the temperature fell to 37·8° within sixteen minutes, and yet no sign of shivering could be observed. That shivering does not occur either even in animals that have survived much longer is clear in that no such movement was ever seen in animals, such as cat II which was taken from a bath and had its temperature dropped rapidly from a normal level to one much below normal during the process of drying.

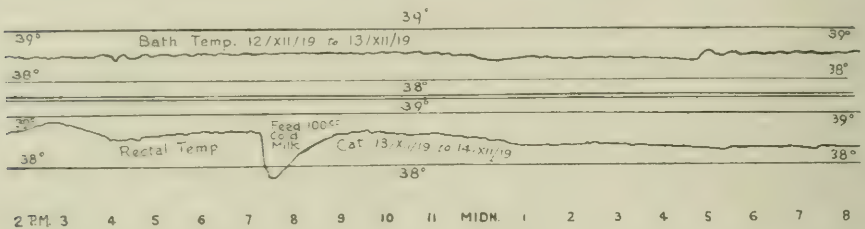

FIG. 5.—Experiment XIV. Abscissa: Time. Ordinate: Temperature. Lower curve: Rectal temperature of animal in bath, December 13 to 14. Upper curve: Temperature record of bath December 12 to 13.

Fig. 5 gives examples of records with a resistance thermometer of the rectal temperature of animal XIV (described a little later) kept in a water bath, as well as a record of the bath itself, the two records being taken on successive days, and the part reproduced includes the early morning hours when the greatest fluctuations of the bath temperature usually took place. The relative steadiness of the rectal temperature by the use of this method is very noticeable, and also the rapid drop of nearly 1° C. in the rectal temperature on feeding this animal (of 2·1 kilo weight) with about 90 c.c. of cold milk by stomach tube. The effect of feeding was always marked, if the food were cold, so that in incubator experiments it was necessary first to warm the milk to the body temperature, since under these conditions recovery of a normal temperature took place much more slowly.

(*f*) *Pseudaffective Reflexes; Mastication and Vocalization.*

Pseudaffective reflexes have already been described by Woodworth and Sherrington [66] in acute preparations, and all those that they have described may be observed in the chronic animal, as well as others which are rarely seen except after survival for a few days. The most common of these reflexes is the lashing of the tail when the animal is touched or stimulated, as by twisting the ear; this reflex is seen in a large percentage of the preparations (both acute and chronic), e.g., cat VIII. Kicking movements and running reflexes may also be induced often by touching an animal, as happened for instance in animals II, IV and V. All these reflexes may be seen in the acute preparation, but they become more common as an animal is kept, and may often be present after the fourth day when the animal has been entirely passive during the first few days. The kicking movements are usually more widespread and general in the later stages than in the earlier, and while they are relatively difficult to induce in the first few days except by strong stimulation of some area on the head, in the later stages mere touch stimuli at any situation will often produce a reaction. Some instances of these may be briefly described.

Animal XIV.—Female. Decerebrated by earlier technique. Had good rigidity with head held to the left, brisk pinna and conjunctival reflexes, pricking of the left ear to auditory stimuli, and it swallowed a stomach tube with a passive reflex action on the first day. By the fourth day the head was raised to the left when sounds were made, especially to such noises as shuffling the feet on the floor, and the stomach tube was only swallowed after apparent objection. This consisted in bending the head backwards, biting, attempts at spitting out the tube and general movements of the head which suggested an attempt to get rid of the tube. The eyes had been washed out with water every day, and on this day it began to "object" to this process, squirming its head backwards and making the washing difficult. On the fifth day there was some conjunctivitis of the left eye and the washing of the eyes was also accompanied by movements of the legs. The section passed just in front of inferior colliculi dorsally to about 3 mm. in front of the pons ventrally. No detailed examination was made.

Animal XV.—Male. Decerebrated by later method. Rigidity good and reflexes good. Slight movements of progression in left hind limb on first day. On second day some progression movements, though slight, in all four limbs from time to time. Stomach tube swallowed passively. No auditory reflex.

On third day on turning the cat over, it had a flexion spasm of both fore paws associated with an increased rate of respiration and some turning of the head to the right.

On fourth day some chewing of the stomach tube but no "objection" to it. A slight nose-licking reflex present after feeding.

On fifth day there was some conjunctivitis. On cleansing the eyes there was apparent objection, movement away of the head and bringing forward of the fore paws as though to push the hand away, but this was badly co-ordinated and ineffective. The condition remained much the same till the eighth day, when the animal "jumped" and showed increase of rigidity on cleansing the eyes but no longer moved the fore limbs. It died from a septic enteritis and pneumonia at the end of the eighth day. The level of the section was symmetrical and passed between the colliculi dorsally to the anterior edge of the pons.

These animals illustrate the gradual change during the first few days with the appearance of reactions not seen at first. Ophthalmia was a common occurrence (due no doubt to their blindness); the apparent objection to the cleansing of the eyes was never seen in the first few days, but was nearly always seen after the fourth or fifth day. During the first few days after operation, the stomach tube is usually well swallowed but without any effort at mastication, after this there is often developed a more complicated reflex, in which the tube is taken with avidity with a well co-ordinated chewing movement which might be so effective as to puncture a stout rubber catheter. Once the tube had reached the stomach the chewing movements would usually cease, to recur again from time to time. It was often noticed that these chewing movements recurred more commonly at a time when milk was flowing through the tube into the stomach. Whether there was any reflex connection between the stomach distension and the mastication reflex is however doubtful, since at this time mechanical movements of the tube in the mouth were liable to occur. On the removal of the tube in a good animal there would occur a nose and mouth licking reflex, usually continuing for two or three licks. A similar nose licking reflex has been described in dogs by Meltzer and Githens [42], and like them we have found that such a response may sometimes be induced by pinching of the nasal septum, but in our preparations it occurs much more regularly as a part of a mastication complex. This nose licking is also very common, even in animals that do not otherwise show it, just before vomiting occurs, and under these conditions some mastication movements usually accompany it.

The mastication movements were usually well co-ordinated and after a few bites food placed near the back of the mouth was swallowed, but the mastication was never sufficient to bite any solid food into small fragments; if the solid food were placed in the front of the mouth it might remain there without any movement occurring, or it might be spat out, or very occasionally chewing movements might be induced. If a number of pieces of solid food were given to such an animal the reflex soon fatigued (a cat is a slow eater) and the bolus of food was left stationary, even though lying at the back of the throat. If such a preparation was then stimulated, as for instance by a slight tap on the nose, it would shake its head, apparently "wake up" and the bolus was immediately swallowed. A mastication reflex was often induced by merely opening the mouth. The position of the section in animals with simple mastication reflexes may be seen by reference to cats III, IV, VIII, all of which showed this reflex well.

After the fifth or sixth day pseudaffective characteristics often appear in this mastication reflex, the tube being apparently objected to as in animal XIV, though food would be well taken. In this reaction it may kick and bite and make the other movements described in the case of cat XIV, or it may be less definite. The sequence of different types of mastication reflex is usually as above, but there are variations, and in our series of 124 complete decerebrations we have had two which showed this seeming objection even on the first day. This was the case with animal XII already referred to, and also in the case of a kitten of 1·7 kilo weight (cat XVI) in which the section passed between the colliculi to the anterior end of the pons. It will be noticed therefore that in these cases the sections were at a normal level.

In many cases the mouths of the animals were washed with 1 in 60 carbolic for cleansing purposes. This process has also been accompanied by a seeming objection, shaking of the head, movements of the limbs, &c.; this reflex also has not been seen during the first few days.

Though the reflexes so far described seem superficially to have some relationship to emotion, they are clearly, even to a casual observer, merely pseudaffective, since they differ from many spinal reflexes only by being rather more elaborate, and since in such a decerebrate animal they appear with a mechanical precision whenever the animal is put under the same conditions. It is also very noticeable that a preparation that appears to object strongly to having its eyes washed will allow the wound on its head to be picked up roughly with forceps while a stitch is passed or removed, and not a movement of its limbs may occur, though a simple rigid extension is maintained. To the stimulus of a foreign body in the eye it has an habitual reflex response, but the puncture of a needle in the scalp is an abnormal stimulus unconnected with any habit or reflex. We can therefore unhesitatingly confirm Sherrington's interpretation of these phenomena.

A type of pseudaffective reflex very rarely seen except in chronic preparations is vocalization. This was only seen in a small percentage of the animals, occurring in ten out of the series of 124 operated on·

Of these ten animals four purred, and where purring occurred at all it was usually repeated. An example is described below.

Animal XVII.—Male kitten, weight 1·3 kilo. Post-mortem see p. 248. Decerebrated by earlier technique. Reflexes fairly brisk and moderate rigidity on second day. On fourth day purred after feeding. This commenced about five minutes after the end of feeding and would then continue for a considerable time. Purred after each feed till the sixth day. When touched would stretch out claws. Occasionally spontaneous purring occurred in bath. On sixth day head wound suppurating and purring reflex no longer seen. On seventh day reflexes very sluggish, even swallowing reflex being poor. Stomach tube inserted in consequence into trachea and 70 c.c. of milk poured into it. (In the ordinary reflex animal it is practically impossible to put the tube down the trachea owing to the swallowing reflexes.) Considerable dyspnœa after this. When fed again, eight hours later, reflexes still very bad. but on stroking the chin after feeding it commenced to purr, but this only lasted about a minute. On ninth day the wound suppuration was improving and reflexes much more brisk. Purring again after morning feed. On tenth day reflexes very dull, respiratory rate very fast and no purring. Death later in the day from lung abscess and empyema, obviously resulting from the passage of milk into the lung.

Animal XVIII.—Young female, weight 2 kilos. Decerebrated by earlier method. Auditory reflex and purring after food present on first day. Vomited and died of suffocation on first night. Section through anterior part of inferior colliculi.

The occurrence of purring with regularity after feeding was very striking and it could not be induced in any animals in any other way. Possibly on the seventh day in cat XVII the stroking under the chin assisted in the development of the response, but it is unlikely, since this form of stimulus was often tried and never at any other time with success. On the other hand, food in the stomach formed the stimulus for the purring in three out of the four animals; the fourth in which it developed spontaneously will be described in more detail later. The disappearance of the purring after food in cat XVII with the development of suppuration in the wound, its return as the wound condition improved, and its disappearance again with the development of the lung abscess was very noticeable, and is of interest in that the animal was kept in a bath, so that the body temperature remained fairly constant, except that the animal was once taken out and dried in an incubator. Purring was observed with a rectal temperature as high as 39·2° C. in the bath and as low as 36·5° in the incubator, while the temperature during the time that purring was absent was about

39·2°, so that it was not change of temperature that caused the purring to cease. With infection, however, there is evidence of the dulling of this reflex, much as infection will diminish spinal reflexes in man or decrease the appetite. But the condition in these preparations is very different from real appetite, since though the purring occurs after food, no sign of even a pseudaffective response is observed if food is withheld.

Animal XIX.—Young, weight 2 kilos, sex not noted. Decerebrated by earlier technique. After operation had good rigidity, good reflexes, head kept to left. Maintenance of good sitting posture lying on right side. No auditory reflex. One and a half hours after operation put into bath and showed repeated strong movements of head to left resembling a clonic movement. After two and a half hours found in bath clawing at the stirrer, all claws extruded but animal purring. On handling it made violent kicking and running movements, and in this kicking its head fell under water. After this it gave two loud co-ordinated mews—not those of pain so much as those of an angry cat. It was taken out of the bath and wrapped in a towel, when it purred again for a while. It was then put back into the bath, when it had no further movements but commenced to purr again. Reflexes and rigidity good. Slight movements of head to acoustic stimuli now present. Later it commenced kicking movements again, but was hobbled. Sounds appeared to increase the movements. When fed it swallowed the tube normally and no purring was noticed after. The wound was restitched with no reaction by the animal occurring. It died during the night, possibly from hyperpyrexia as the result of violent exercise in the hot bath.

Autopsy showed a slight intracranial hæmorrhage (about the size of a small pea) and the section passing through the anterior half of the superior colliculi to 2 mm. in front of the pons, the section being slightly oblique with rather more removed on the left than on the right. All the nervous tissue above had been completely removed. Histological examination was not possible owing to post-mortem softening.

This animal appeared to have vocalization reflexes occurring immediately after operation in a more or less disorganized form. It will be evident from the three examples quoted that the level of the section has been rather anterior, and it might have been concluded that the reaction depended on centres lying above the level of the pons. But another cat which purred (cat XX) seems to disprove this.

Animal XX.—Female, weight 2 kilos. Decerebrated by earlier technique. Rigidity good. No auditory reflex. Purred after feeding on the third day, and repeated this after all meals until it died at the beginning of the fifth day. Cause of death uncertain, though there was superficial infection of the wound.

The section passed through the lower parts of the inferior colliculi to the upper edge of the pons. No histological examination attempted owing to post-mortem softening of the brain.

It seems to be therefore established that purring reflexes depend on reflexes through centres in the medulla—though such centres are probably high in the medulla, since the reaction is usually not seen for the first few days after operation, and shock is probably more prolonged in the immediate neighbourhood of the section. It is noticeable that purring was only seen in young animals, and then usually in females, all animals which might be expected to purr readily during life, and in which there may have been a purring habit. The possibility of a medulla-initiated habit is strengthened by a consideration of those animals in which vocalization in the form of growling occurred.

Growling was observed in three animals, and shows considerable contrasts when compared with the purring reflexes. All three animals were adult males, and two of them old scarred animals which had evidently done a lot of fighting. The sound was exactly that made by a cat when fighting, and none of the animals made the sound more than once. In one case it was made on the fourth day when the animal's mouth was being cleaned with carbolic; in another (cat XXI—for description see page 221), about two hours after operation as a reaction to air blown into its ear: and in the third (cat III already described) it occurred about three hours after the operation, when the animal was put into the bath. None of the animals repeated the sound (even though cat XXI survived for twenty-two days), however much they were subjected to nocuous stimuli.

Here, again, the vocalization was of a type suggesting that habit formed an important factor, but in this case the sound occurred as an isolated phenomenon, and was not repeated in a reflex and automatic manner as was purring.

Cat III was peculiar in that it gave this growling sound on the first day and no more sounds till the sixth day, when it made a sound somewhere between a growl and a mew while having its temperature taken with a rectal thermometer, at the same time making kicking movements which have been described already. The insertion of a rectal thermometer was an occurrence which was often repeated, and yet only evoked this reaction once, and the same animal on the seventh day gave a series of ten loud and well co-ordinated mews when being turned on its mattress—another response which it could never be persuaded to repeat. At the end of the seventh day it died—the exact cause being uncertain.

An indefinite cry somewhat similar to a mew has been observed in five animals, of which cats II, III, X and XXI, supply instances. In the other instance the sound occurred once on putting the animal into the bath on the first day ; in this animal the section was anterior, from the anterior end of the colliculi to 1·5 mm. in front of the pons, though operated on by the later method. In the case of this sound repetition was occasionally seen, but it could never be reproduced consistently as could purring. This cry is probably similar to the cry made by an animal under an anæsthetic, and which Sherrington [55] [66] has described as occurring also in decerebrate animals while anæsthetized. A normal mew was only observed twice—in cat III, as described above, and in cat XIX, of which details have been already given. In neither case was the mewing repeated, nor could it be produced by subjecting the preparations to nocuous stimuli.

One preparation must now be briefly described to give a clearer picture of the mode of occurrence of pseudaffective responses in general :—

Animal XXI.—Long-haired male ; weight 2·5 kilos. (For post-mortem see p. 246). Decerebrated by older method. Had good rigidity one hour after operation, but no good sitting posture adopted. No movements made. Head kept to the left. On putting into bath two hours after operation and blowing into ear when it lay on right side, left pinna retracted, head raised to left and slight low growling sound made. On third day rigidity good, some doubtful pricking of ears to sounds. On fourth day began to kick a lot when turned. On sixth day respiratory rate irregular—about 30 per minute—quickening when the animal was touched. For the first time showed apparent objection to swallowing of stomach tube. On eighth day apparent objection to cleansing of eyes and mouth. Considerable kicking movements when turned, running movements when rectal thermometer inserted. While having eyes cleansed twice made an indefinite cry. Mastication reflexes good—chewed and swallowed piece of meat put into very front of mouth, but on repeating spat second piece out. On twelfth day made movements of resistance against any interference with the position of its head. On thirteenth day respiratory rate raised after turning (apparently as the result of reaction to handling) to 36, to drop to 24 on leaving the preparation undisturbed.

The condition remained as above, but without any more sounds being made till the beginning of the twenty-second day, when the rigidity became less and the reflexes duller, the animal dying at the end of the day.

(*g*) *Spontaneous Movements.*

Spontaneous movements in the form of progression as well as movements of the pseudaffective and defence type have already been described, and it is clear that a distinction must be drawn between the progression movements and pseudaffective responses found after a section through the inferior colliculi to just in front of the pons and those seen when the section was 1 to 3 mm. more anterior, especially on the ventral aspect of the brain-stem. In the former, the pseudaffective responses usually developed only after two to four days, and though they gradually became more active (e.g., cat II), they were never violent. In the latter (as in cat XIX) these movements were seen soon after operation and were much more violent.

Nothing can be added to the description of this second type of animal already given by Woodworth and Sherrington, except to draw attention to the exceptional case with vocalization (cat XIX) already described, and to note that on two occasions such animals have raised themselves from a lying to a standing posture in the incubator and have been found leaning upright against the side of the incubator. Three animals may be briefly described.

Animal XXII.—Female. Decerebrated by older technique. Nystagmus to right and jerky movements of head to right immediately after operation. One hour later found standing in incubator, leaning against side and attempting progression. It died shortly after this. The section was anterior to the superior colliculi and 7 mm. above the pons ventrally with many small punctate hæmorrhages in the mid-brain above the level of the middle of the posterior colliculi. There was a considerable amount of blood-clot lying around the cerebellum and medulla.

With this animal may be compared another (XXIII) in which the section, though low posteriorly, was anterior on the ventral aspect, and one (XXIV) anterior both on the dorsal and ventral aspects.

Animal XXIII.—Adult male. Post-mortem, see p. 248, and figs. 22 and 23. Decerebrated by older technique. Rigidity good. On second day on cleansing the mouth with carbolic it kicked violently and moved about a great deal. The respiratory rate remained about 19 to 28 during "life"; it was constantly making progression movements spontaneously, but only kicked violently when touched. Died on sixth day.

Animal XXIV.—Female. Decerebrated by older technique. Three-quarters of an hour after operation found standing in incubator leaning against the side with its head down biting the wire netting floor. It was making violent kicking movements. It was taken out of incubator and then remained quiet, but showed auditory reflexes. After another forty-five minutes it was put into the bath, when it again had a paroxysm of most violent movements. It died about four hours after operation. The section passed through the superior colliculi and was 4 to 6 mm. in front of the pons ventrally. There were three small punctate hæmorrhages in the mid-brain just below the posterior colliculi, and considerable subtentorial hæmorrhage extending around the cerebellum and medulla and some way down the cord.

The movements in these anterior sections recur in paroxysms every fifteen to forty-five minutes, the intervals being shortened if the animals are exposed to stimuli such as touches, shakes or sounds. On the other hand, immediately after such a paroxysm there is a refractory quiescent interval, and in such an interval an animal of this type will lie quietly passive in a condition of simple decerebrate rigidity while a wound is stitched, although fifteen minutes later it may react with the utmost violence to a slight stimulus such as a jar or sound. Here, again, there is no evidence at all of any conscious sensation or emotion.

In these animals the movements usually resulted in reactionary hæmorrhage and it has never been found possible to preserve them for more than a few hours. A contributory factor to their death may well have been the respiratory irregularities described by Macleod [34], though in our animals movements were so active and general that it was not possible to judge whether there was any hyperpnœa other than that secondary to the exercise.

Slight vomiting just before death was in these a common occurrence.

Of other movements that have been observed two are worthy of notice. One has been described in cat II—an apparent attempt to reach a sore spot on its skin with its fore-paws, and the other was a complex scratch movement made by cat XIII, which four hours after operation curled itself up into a flexed position, although it had good extensor rigidity, and made (almost completely) the movement used by a cat when scratching the back of its neck with one of its hind limbs.

It is noticeable that violent movements and vocalization were only seen in one animal out of twenty-seven operated on by the later technique. In the latter technique the section had a different obliquity, passing usually from just in front of the corpora quadrigemina to just *below* the anterior border of the pons, and in the one exception where violent pseudaffective movements were made soon after operation and where an indefinite cry was also made, the section had passed just in front of the superior colliculi to 1·5 *millimetres in front of the pons.* The centres responsible for this reaction therefore probably lie nearer the ventral than the dorsal side of the brain-stem, since it is the level of the section on the ventral aspect that makes the most difference (contrast however cat XXIII). And yet the animals operated on by the later method showed the other more common pseudaffective responses and were very liable to make progression movements, in spite of the different obliquity of the section.

(*h*) *Acoustic Reflexes.*

Acoustic reflexes have been described in the case of animal II and a similar lifting of the head to the left was also seen in cat III, commencing about two hours after operation, and some such reflex was also present in VI, IX, XIV, XVIII, XIX, XXI and XXIV of the animals so far described and also in animal XXVI to be described later. No doubt the other acoustic reflexes described by Forbes and Sherrington [14], such as wagging of the tail in response to high notes, may have occurred in many of the animals, but their position in the bath was not favourable to its observation and it was only noticed in a few animals. Movement of the head and of the fore-limbs was observed in many animals and was usually particularly noticeable, as in animal II, in those cases where the rigidity of the neck muscles was uneven so that the head tended to go to one side or the other. Apparently the stimulus increased the rigidity, and this being uneven, movement of the head resulted. In no case did an animal raise its head to sounds regardless of the position it was lying in; invariably the head was only moved to one side or the other.

The auditory reflexes became usually much more brisk after two or three days, and might often be seen at this stage when there had been no sign of them earlier, so that their absence could not be presumed unless the preparation had survived at least three or four days.

The greater reaction to high notes, resembling the roof-cries of cats, noticed by Forbes and Sherrington, was often confirmed; on the other hand, in many animals the most effective sound was a small scratching noise, and an animal would often react promptly by raising its head if a piece of paper was crumpled up at a distance of one or two yards· These sounds are similar to those made by a mouse. One reaction to sounds sometimes observed was the extrusion of the claws in the fore-limbs, which may perhaps be a guide to the nature of the reflex. Animals would react to these slight noises even though there was a constant loud noise from the motor and stirrers, to which no reaction was shown except when it was started after an interval of rest. It is worth noting that in the older technique a reaction to sounds was noted in most animals where the section passed in front of the inferior colliculi to about 2 mm. in front of the pons, but even so not in all, and that it was seen in one in which the section commenced in the middle of the inferior colliculi and passed to the same level. It was never seen in sections by the later method with a different plane of section, if this passed from the anterior end of the superior colliculi to the anterior end of the pons, but was seen in one case where the section passed from just in front of the superior colliculi to 1·5 mm. in front of the pons, in the animal which has been referred to as having spontaneous violent movements and vocalization. It would appear therefore that here too the level of the section ventrally makes more difference than the level of the section dorsally, and that the highest link in the chain for this reflex may be nearer the ventral than the dorsal part of the brain-stem.

On the other hand, in cat XXIII (see figs. 22 and 23 and p. 248), no auditory reflex was observed, though the section was anterior on the ventral aspect.

(i) *Nystagmus.*

Spontaneous nystagmus was seen in several preparations, but usually in the first few hours only after operation, and probably as the result of irritative effects of hæmorrhage.

In animal XXII already described there was a jerky movement of the head to the right accompanied by nystagmus, which was kept up spontaneously during the few hours of life.

Two animals may be briefly described.

Animal XXV.—Adult male. Decerebrated by earlier method. Two and a-half hours after operation had extreme rigidity and made running movements when touched. Five hours after operation had paroxysms of violent fighting movements, claws extended, springing movements also made. General appearance of anger, but all movements inco-ordinate. Several paroxysms at about fifteen-minute intervals. Pinna reflexes brisk. No definite auditory reflexes. Just before the attacks there was some increase in the already very great rigidity, with some retraction of the head, which was also bent to the left. With this there was nystagmus to the left and jerky movements of the head to the left, present to a slight extent all the time, but exaggerated with the commencement of a paroxysm. Animal died in the night, vomiting slightly before death. The section passed in front of right superior colliculus and through the middle of the left superior colliculus dorsally to emerge

3 mm. in front of the pons on the right and 1 mm. in front of it on the left. There was no sign of hæmorrhage into the stump of the brain-stem but a clot about the size of three peas was lying over the stump above the tentorium. No detailed examination was made.

Animal XXVI.—Female. Post-mortem, see p. 249. Decerebrated by earlier technique. Good rigidity, head to left, good reflexes, lifts head to left to noises on first day. No nystagmus.

On second day head lifted to left in reaction to sounds and this accompanied by nystagmus to left.

On third day respiration very fast. Reflexes very sluggish and almost absent. Some convulsive movements of the legs, but no eye movements. Died during the night.

The nystagmus when seen was of a usual type with rapid and slow components, but the animal described above and animal IX which developed nystagmus on the ninth day when meningitis occurred were the only ones where it has been observed, except in the first few hours after operation.

(*j*) *Glycosuria.*

It has been suggested by J. Mellanby [41] that there is a centre in the brain above the medulla which controls sugar metabolism, this theory having been built up on the prolonged glycosuria which follows decerebration as compared with that seen after decapitation. But Mellanby's decerebrate preparations were made by Langley's [29] starch injection method, so that nothing definite was known of the real level of the lesion, nor of the changes resulting in the pituitary. At the same time the glycosuria observed was only investigated over a matter of a few hours after operation. We can, however, amply confirm the long duration of glycosuria found by Mellanby after decerebration; thus in one animal urine obtained by catheterization from the bladder twenty-four hours after decerebration still contained quantities of sugar.

On the other hand, the glycosuria does not continue indefinitely. Thus the urine of cat VIII contained no sugar on the third day; in another animal (XV) urine voided forty-seven hours after operation contained no sugar. This animal had previously voided fæces and urine about thirty hours after operation; so it appeared to have ceased to secrete sugar, at any rate after thirty hours. In no case has any glycosuria been observed after the second day—though observations on this question have only been possible in preparations kept in the incubator. Nor does it appear possible that the glycosuria ceases as the result of loss of glycogen. In cat V urine collected on the sixth day showed no sign of sugar, and yet when the animal was killed shortly afterwards the liver gave a normal glycogen reaction with iodine. In cat XXI, urine taken from the bladder after death contained no sugar, but the liver was not normal.

The theory put forward by Mellanby does not, therefore, explain the facts—though the more prolonged glycosuria compared with that of the decapitate preparation certainly requires some explanation. Further, experiments on this point are planned for the near future. The glycosuria we have observed occurs even when the body temperature has been subnormal for quite a short while, and we do not think that it is to be explained as merely secondary to a fall in body temperature as is suggested by the experiments of Morita [44] on rabbits: nor do we find, as he did, that it ends usually only cn exhaustion of the liver glycogen.

CHAPTER IV.—UNILATERAL DECEREBRATION.

A series of semi-decerebrations as chronic experiments was undertaken on the suggestion of Professor Sherrington, in order to study the resultant decerebrate rigidity. Seventeen cats were operated upon of which four died at once from hæmorrhage or accidents of anæsthesia. The remaining thirteen experiments are not sufficient to answer many of the questions that prompted the undertaking, and further work has been planned along the same line. It seems worth while, however, to include here a brief description of the semi-decerebrate preparations for the sake of comparison with the results of complete decerebration.

Operative Technique.

Cats were used under chloroform or chloroform and ether anæsthesia by the open method. A small mid-line incision was made in the neck and the right carotid tied. The left carotid and vertebrals were controlled at the proper time as in the bilateral operation. The skin and muscle were reflected from the right side of the head. The underlying skull was quickly removed so as to expose the right cerebral hemisphere. The dura was reflected. Then, with the arterial supply shut off, the operator passed a flat bone spatula (a properly shaped saltspoon) over the top of the right cerebral hemisphere, until it touched the falx, and swept it downwards to the tentorium and outwards, carrying away all of the hemisphere except the frontal pole, which could be quickly scraped out. A part of the inferior colliculus was usually thus left intact. This was reflected forward from the surface of the cerebellum and removed by a bent bistoury, together with any of the mid-brain that may have remained ventrally above the top of the pons. The cavity was quickly filled with cotton wool in hot saline and the vertebral arteries released. Bits of fresh muscle were usually necessary to arrest all bleeding before the left carotid artery was released. The cavity was filled with physiological saline before closure.

In six of the experiments the cavity was filled with a melted paraffin-vaseline mixture after removal of the hemisphere. One of these animals lived only eleven hours, and four died on the day following operation. Three of the animals became dull and vomited just before death. Compression beneath the wax was suspected, and when the sixth animal became dull two days after operation the wound was opened and the paraffin removed. There was a gush of fluid from beneath showing increased pressure. The animal improved temporarily, but died on the day following from broncho-pneumonia. Examination of the brains where the dead space was filled with saline, as described above, showed a varying amount of swelling of the remaining hemisphere across the mid-line. The animals whose cranial cavities were filled with normal saline rather than wax lived to between two and forty-two days after operation. The conclusion is evident: that swelling of the remaining brain tissue against the wax was sufficient to cause fatal compression of the lower centres.

It was found advisable to suspend the more active animals in a hammock provided with slits for the legs to come through.

The removal, which was always on the right side, extended in each case down to the mid-brain. Two types of removal were made: (1) anterior, where the decerebration passed above the inferior colliculus, leaving a varying amount of superior colliculus intact and most of the mid-brain ventrally (in this type the red nucleus was not molested); (2) a posterior removal where the section passed from behind the inferior colliculus dorsally, to the anterior margin of the pons ventrally. In this type one red nucleus was removed. Post-mortem examination showed that the removal followed the median sagittal plane with surprising accuracy, except for the fact that in two cases the spatula passed about 2 mm. to the right of this plane, leaving that thickness of mid-brain and thalamus, and in several cases a very small amount of the left thalamus or mid-brain was removed.

Forced Movements and Attitude of Head.

The animal's head was *usually* held to the left at the close of the operation, and in *every case* eventually. This attitude depended on rotation of the occiput downward and to the left, so that the chin was up on the opposite side and the neck bent to the left. The displacement therefore consisted of retraction of the neck and clockwise rotation of the head on the shoulders, the head being carried to the left away from the side of removal. Those that were able to walk fell to the left or walked around in a circle to the left. If the animal was laid on its right side it raised its head up to the left and, pushing with the right fore limb, rolled about the cage. When lying on the left side the preparation frequently lay quietly but pressed the occiput against the floor. These attitudes were eventually assumed in every case (except that in two animals no note was made of any forced circus movements). In all of the anterior sections, as described above, and in the one posterior section where about 2 mm. thickness of the mesial portion of the mid-brain and thalamus were left intact, the animals turned their heads first to the right on recovering from the anæsthetic. Within one to five hours in each case this movement was reversed and the typical movement of the head to the left appeared, associated with forced movements to that side. The short duration of this preliminary turning to the right in the anterior section cases before reversal suggests that some structure is spared by the anterior or lateral removal, which is stimulated by traumatic irritation, but later becomes paralysed or unable to cope with a contrary tonic influence.

After the effects of stimulation had passed off, the head was held constantly in a position similar to what has been termed the cerebellar attitude. In lesions of one side of the cerebellum, the occiput is said to turn in that direction and the head to be retracted to the side of the lesion. In semi-sections of the mid-brain, at either a high or a low level, the movement is *away* from the lesion. This was a constant finding in these experiments. It may be explained perhaps by the fact that one side of the cerebellum is in close anatomical relation with the other side of the mid-brain. Muskens [45] has made extended observations on the effect of lesions confined to the posterior longitudinal bundle. Circus and rolling movements followed such injuries. It is difficult to make explicit applications of his results to the movements described here however.

The Side of Permanent Extensor Rigidity.

Sherrington noted in 1898 [54], working with acute experiments, that unilateral decerebration through the mid-brain was followed less regularly by decerebrate rigidity than complete sections of the brain-stem. It appeared most often on the same side as the decerebration and was occasionally observed to subside and reappear. He noted in a monkey and in cats that after right semi-decerebration, the right limbs were held in tonic extension, the tail incurvated to the right with the concavity to the right. The head was turned to the right and retracted. The left fore limb and knee were distinctly more flexed than would be expected in paralysed limbs. Thiele [57], in acute experiments, likewise noted ipsilateral rigidity after semi-section of the mid-brain, and that if the section were more anterior, through the superior colliculi, the rigidity tended to become *contra*-lateral, only a little remaining on the ipsilateral side.

The chronic experiments described below show that some of the above post-operative reactions are reversed after an initial stage of stimulation.

In the following experiment, No. P1, after removal of the right hemisphere down to the mid-brain, the preparation was suspended in a hammock in erect position with legs passing through hammock holes. The animal's head was at once turned to the right and there was extensor rigidity in all four limbs. There was slow nystagmus with the quick component to the right. At intervals there were spasms of running movements during which periods the nystagmus became more rapid. The rigidity of the left limbs became progressively less marked until two and a half hours after the close of the operation, when the right fore and hind limbs were found to be still in tonic extension sufficient to support the weight of the body. Both left limbs, however, tended to assume a flexed posture and were held thus a little rigidly. The spontaneous nystagmus had disappeared. At intervals spasms came on resembling those mentioned above, except that now the right limbs ran and the left limbs became still more flexed, especially the fore limb. At these times the eyes opened, the head turned to the right, and there reappeared a very small amount of nystagmus to the right. Left pupil widely dilated, right pupil less so. Rectal temperature 37° C.

Four and a half hours after operation—head was now turned constantly to left.

Twenty-four hours after operation—head to left and body, including tail, curved with the concavity to the left. Extensor rigidity marked on right side. Left limbs held in tonic flexion so as to resist passive extension. Occasional clawing spasms, at which times the head was retracted. The preparation was taken from the hammock and it swallowed some milk which was poured into its mouth.

Three days after operation there had occurred a surprising change. The extensor rigidity was now in the left limbs. When suspended in the hammock and quiet, the right limbs maintained a flexed position. It was not possible to say whether there was any flexor tonus however, as the right limbs were now voluntarily snatched away when touched and were used to scratch the observer's hand whenever he attempted to administer food. The left limbs were never used in this way. When placed on the floor the animal walked slowly in a circle to the left, reeling and falling to the left. The head was still held to the left and the jaw tightly clenched. The pupils were now equal. Temperature 38° C. Late the same night condition unchanged.

Four days after operation. The front end of hammock had fallen, so that the animal's head hung almost straight down. Animal dead.

Post-mortem: A subdural hæmorrhage was found extending over the left hemisphere, under the base of the brain and down the cord to the upper dorsal region. Some of the hæmorrhage appeared to be more recent than other parts. The operative removal extended back to the middle of the inferior colliculus but had not quite come to the mid-line, so that 2 mm. of the mesial part of the mid-brain and 3 to 4 mm. thickness of the posterior part of the right thalamus were spared. A very thin slice of the mesial part of the frontal lobe was likewise spared. Interrupted serial sections were cut of the whole left hemisphere, mid-brain, pons, and medulla. There was no area of destruction or softening.

It seems probable that the behaviour of the cat immediately following the operation was due to stimulation which gradually subsided during the succeeding two days. During that time various reactions disappeared or were replaced by opposite reactions. The early rhythmic intensification of these reactions also suggests a response to irritation, i.e., clawing or running spasms associated with nystagmus to the right, head turning to the right and increase in the left-sided flexor rigidity. The spontaneous nystagmus disappeared a few hours after operation. The head, which had been first thrust to the right, came later to the mid-position and shortly afterwards was turned to the opposite side, to remain constantly in this typical position with corresponding curving of the body to the left. The occasional spasms of running movements continued for two days. At the end of that time the flexor rigidity of the left limbs disappeared and was replaced by extensor rigidity; while the extensor rigidity disappeared on the right side to be replaced by the position of flexion in the right limbs when at rest.

The unusually long duration of the signs of stimulation may possibly be explained by the evidence of older hæmorrhage at autopsy, which had not been enough to cause compression until the accident which led to the animal's death.

Shortly after operation this animal resembled those described by Sherrington in acute experiments. Extensor rigidity was present on the same side as the decerebration, but *after* the irritation stage had passed off it was on the contralateral side. The same was true of all other animals where the section passed through the anterior part of the mid-brain. Extensor rigidity appeared on the contralateral side either at once or after a preliminary stage of flexor rigidity.

Variations after Posterior Semidecerebration.

On the other hand, when the level of removal was through the lower mesencephalon or junction of the mesencephalon and pons, the results were less constant and subject to less symmetrical variations. For example, take the following experiments :—

P2. The removal was of the posterior type. Bilateral-extensor rigidity developed on the first day. On the second day a varying degree of flexor rigidity of the left fore-limb appeared, with extensor rigidity of the other three limbs.

Experiment P3 showed, one hour after operation, extensor rigidity of the left fore-limb, the other limbs being flaccid. At the end of five hours the left fore-limb showed flexor rigidity, the other three extensor rigidity.

Experiment P4. Bilateral-extensor rigidity with considerable retraction of head associated with the usual turning to the left.

Experiment P5. A more detailed account of this animal is given on page 234, but it may be noted here that on the day of the operation there was bilateral rigidity. This was followed by some variation and then for several days, when not moving about, the fore-limbs were held in rigid flexion, the head held to the left and the neck flexed sharply on the fore-paws, while both hind-limbs went into tonic extension. This was followed by weeks of activity associated with a variable amount of extensor tone in the left fore and hind limbs.

This variation in the tone of the flexor and extensor systems in posterior removals suggests that some structure responsible for preserving a symmetrical tone pattern has been injured.

Flexor Rigidity.

After more anterior semi-decerebrations, the post-operative pattern was tonic-extension in the limbs on one side and tonic-flexion in those of the other. In certain cases, e.g., P1, the extensor rigidity appeared first on the ipsilateral side with flexor rigidity on the other side. This was, however, shortly reversed.

It may be suggested in unilateral removal, after all stimulation effect has passed off, that control has been removed from some structure whose unantagonized action produces tonic-extensor rigidity in the contralateral limbs and tonic-*flexor* rigidity on the ipsilateral side. When the decerebration is bilateral the flexor element usually disappears and is superseded by extensor rigidity on both sides. But, as is shown elsewhere in this paper (Exps. III and IV, p. 199), even in the complete decerebration experiments, tonic-flexion occasionally replaces tonic extension.

Thiele [57] and Graham Brown [9] found that electrical stimulation of one side of the mesencephalon in the region of the red nucleus produced ipsilateral flexion and contralateral extension. The latter observed that there was an after-discharge following cessation of stimulation. It is difficult to be certain exactly what tract is stimulated by these workers. Bilateral stimulation produces bilateral extension. Their work indicates that there are structures in the mid-brain, possibly the red nuclei, which take part in the control of posture. (Also Magnus [40].) It is not necessary, nor possible, to identify this postural mechanism with that responsible for flexor or extensor rigidity.

One of the conclusions that may be drawn from these chronic preparations is that there is a mechanism by means of which there may be induced increase of tone in flexor muscles at the expense of tone in the muscles of the extensor surfaces. This flexor rigidity tends to alternate with extensor rigidity, appearing frequently in the limbs of the side opposite to that in which extensor rigidity occurs.

Wilson [63] describes decerebrate attitudes in clinical cases associated with mesencephalic lesions. In his fig. 13, p. 247, the child has assumed a position resembling the attitude of unilateral decerebrate rigidity, with arm and leg of one side extended, as the author points out. It is interesting to note, however, that in addition the limbs of the opposite side are held in a sharply flexed attitude.

Eye Changes.

In every case where the corneal reflex was examined it was present on both sides. There was some variation, but the right pupil was dilated in the great majority of cases. This was most noticeable on the first day after operation. Nystagmus was observed only in one experiment. This was in P1, see p. 230, and passed off with other evidences of stimulation. The quick phase was toward the side to which the head was turned.

Temperature Control.

Most of the animals preserved some power of temperature control if not exposed to extremes. In three experiments there was no evidence of control whatever, the temperature falling to between 34°5 C. and 24°5 C. Those animals which survived longest maintained a normal temperature. In experiment P5 it was noted in a cold room that the animal shivered equally in the limbs of the two sides. In this animal the removal extended down to the anterior end of the pons and was carried well over to the mid-line. Removing the other half of the brain at the same level would have put an end to shivering (see p. 205).

Experiment P5 was described in part above, but as the animal lived forty-five days before being sacrificed, a brief account of the post-operative behaviour may be added.

The right side of the brain was removed up to the mid-line and down to a level below the inferior colliculus. The cavity was filled with saline. After the operation the right pupil was found to be dilated, the left contracted, both corneal reflexes present. For two days there was bilateral extensor rigidity which became variable. The animal was examined by Dr. Henry Head and Dr. Riddoch, who called attention to the fact that when it lay on the left side the left fore-limb was held in tonic flexion with claws extruded, and that ten minutes after turning over on to the right side the right fore-limb assumed the flexed attitude. This was not a constant finding at later examinations. The head was consistently turned to the left and the body and tail curved with concavity to the left. Milk was swallowed when placed on the back of the tongue with a tube. The animal clawed with right paws only. On the third day the fore-limbs were flexed sharply and paws crossed with the head bent down upon them and with occiput a little to the left. Both hind limbs were extended strongly most of the time. When disturbed there resulted spitting and clawing or purring appropriately. This continued for four or five days with gradually increasing activity. During the first week the temperature fluctuated between 40° C. and 37°8 C. After this the temperature settled down to normal, about 38°6 C.

Between one month and six weeks after operation the following notes were made. The cat had gained in weight. The head was rotated still, with occiput to the left and chin to the right, the neck, body and tail being curved with the

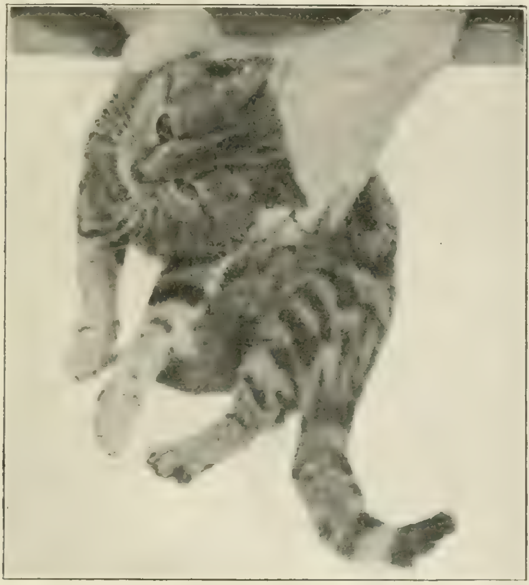

FIG. 6.—Experiment P5. Six weeks after complete removal of right side of brain, including mesencephalon. Tail curved to left, left legs extended, toes of left hind paws fanned, both fore paws rotated with pads a little towards the right. All of these attitudes are characteristic, as well as the rotation of the head on the shoulders.

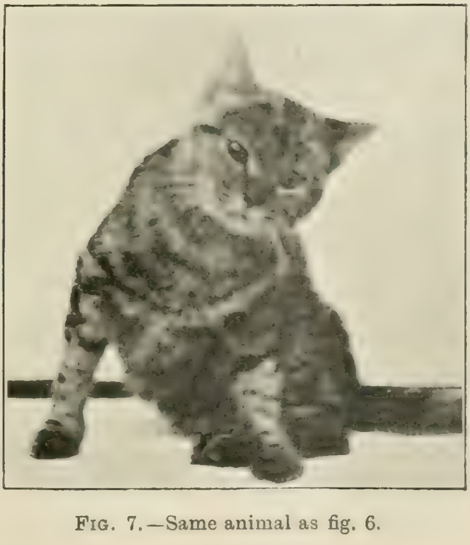

FIG. 7.—Same animal as fig. 6.

concavity to the left (see figs. 6 and 7). When not lying quietly, the animal walked around in a circle to the left. She purred frequently and growled or spat occasionally. Even when restless from hunger, she never discovered meat or milk placed before her unless her nose was pushed down into it, resembling Goltz's dog in this respect. After she realized what it was, she ate or drank almost normally until satisfied.

Cranial nerves: She gave no evidence of smelling food from any distance but may have done so at close range. She was blind, bumping into objects frequently or walking off the edge of a board unawares. Her eye grounds were examined by Mr. Leslie Paton, who made the following note: Right optic disc chocolate colour with a sharply defined ring of very glistening green around it. Vessels normal in calibre. Upper part of fundus shows a little speckling of green passing down to a deeper green in the lower part. Left optic disc much the same as the right. The eye movements were examined by Dr. Gordon Holmes. The external ocular movements were normal and the range to either side seemed to be full. The right pupil did not react either directly or consensually to light, while the left pupil contracted to light in either eye. The right pupil did contract with some movements of the eyes, however. Also, tickling the nose or blowing into the eye caused very definite contraction of the right pupil. Reaction to pin prick and corneal reflex indicated intact fifth nerve on both sides. Hearing was acute and sounds were well localized. All other cranial nerves appeared normal.

Extremities: There was considerable variation but on the whole there tended to be tonic extension of the limbs of the left side (the opposite side to the removal). When suspended, the left limbs were extended and the hind toes fanned (see fig. 6). The left fore-paw was inverted and the right fore-paw everted. The knee jerks varied but the left was usually the more brisk.

Sensation: Pinprick was resented equally on the two sides. Touching the hair on the right side produced a reaction. The same stimulus on the left flank was ignored.

Heat control: Shivered symmetrically when in a cold room.

Gait: The right fore-foot took a longer step than the left and the foot was raised higher. She turned in a large circle to the left. Occasionally she stepped on the dorsum instead of the plantar aspect of the left fore or hind paw, and the left hind-paw at times interfered with the fore-paw. When excited, she walked about in a very small circle. It was noted by Dr. S. A. K. Wilson that the left fore-foot was advanced at each step with a tremor of the paw. At times she stumbled to the left.

Affective reactions: She purred when stroked or after feeding, growled when eating meat, and occasionally spat and scratched. When another cat was brought near her, no notice was taken until the visitor mewed. Then P5 growled and became suddenly rigid as though listening. After a little time she started toward the visitor who was moving softly, and continued until her nose bumped into the visitor. Then P5 leaped back and stood with all hair raised on back and tail. The visitor moved away and at that moment P5 struck out as though to attack her, spitting. The visiting cat was removed and P5 walked around very rapidly in a small circle.

Six weeks after the operation, the animal in excellent physical condition was sacrificed under ether-anæsthesia. Post-mortem examination showed the right side of the brain to have been thoroughly removed up to the mid-line. Several shreds of what may have been cortical tissue were left. These were not connected with the brain-stem. The right thalamus and mid-brain were removed down to a plane which passed through the anterior margin of the pons ventrally, and just behind the inferior colliculus dorsally. A complete microscopical report could be made as an unfortunate accident destroyed most of the material while it was being prepared.

Chapter V.—Microscopical Anatomy of Specimens.

(*a*) *Development of the Mid-Brain.*

In lower vertebrates (e.g., fishes) the mid-brain is a centre of great importance, controlling the individual response to environment. With the development of the optic thalamus and the geniculate bodies (reptiles) the importance of the mid-brain for co-ordinating visual stimuli is decreased, and in man with the elaboration of the visual cortex the anterior corpora quadrigemina of the mid-brain become rudiments. There is likewise a forward displacement of the sensory centres to the ventral part of the thalamus, which continues to develop along with the sensory cortex. The auditory paths move out from the mid-brain to the internal geniculate body and auditory cortex. The mid-brain has therefore a progressively decreasing functional importance proportionally during phylogenetic development.

Microscopically the red nucleus of a lower vertebrate is composed of large cells of motor type from which arise the rubrospinal tracts. Higher in the phylogenetic scale there appear smaller cells in the red nucleus and, as von Monakow [43] has pointed out, it is possible to distinguish an orally placed group of smaller cells, the nucleus parvicellularis of Hatschek [19] or chief nucleus, from the more caudal giant cells, or nucleus magnocellularis. The small-celled nucleus develops *pari passu* with the thalamus and cerebral cortex and is connected with them. In anthropoids and man this nucleus of small cells makes up the major part of the red nucleus, while the giant-celled part has become very small and, as a result, the rubrospinal tract has greatly diminished in volume. Nevertheless, because of the great increase in size of the small cell part, the red nucleus of man is almost twice as large as that of the cat in proportion to the vertical diameter of the mid-brain of each species [43].

(*b*) *Anatomy of the Mid-Brain.*

The anatomy of the mid-brain of a cat may be quickly reviewed by reference to fig. 8, which is a drawing from a lateral longitudinal section through a cat's brain. It will be seen that a section through the mid-brain may leave or remove according to its level a number of structures, the anterior and posterior corpora quadrigemina, the third and fourth cranial nerve nuclei, the whole of the tegmentum, the red nucleus, &c. The red nucleus is circumscribed by a felt-work of fibres. The caudal two-thirds of the nucleus is made up of giant cells as indicated. The oral one-third only is made up of small cells.

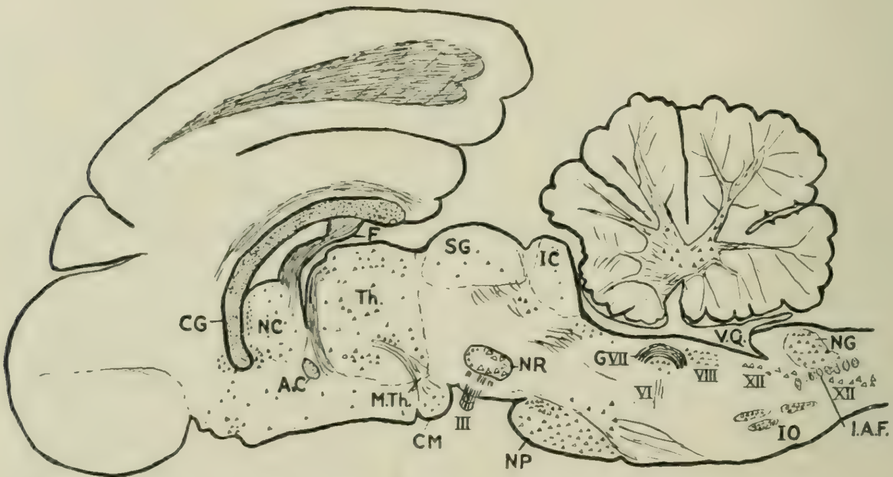

FIG. 8.--Sagittal section of cat's brain a few millimetres from the median plane, drawn from two adjacent sections, one stained by Loyez's hæmatoxylin method and the other by Nissl's method. This as well as all the other microscopical drawings was made with the help of an Edinger Drawing Apparatus kindly loaned by Dr. Gordon Holmes. Diagrams in succeeding figures are taken from this drawing reduced to natural size. C.C., corpus callosum; N.C., nucleus caudatus; A.C., anterior commissure; F., fornix; Th., thalamus; M.Th., mamillo-thalamic tract or bundle of Vicq d'Azyr; S.C., superior colliculus; I.C., inferior colliculus; N.R., nucleus ruber; N.P., nuclei pontis; III, root of III nerve; G VII, genu of VII nerve; VI, nucleus and root of VI nerve; VIII, dorsal nucleus of VIII nerve; XII, nucleus of XII nerve; V.Q., fourth ventricle; I.A.F., internal arcuate fibres splitting XII nucleus.

According to Hatschek, this phylogenetically younger nucleus parvicellularis is in relation with the nucleus dentatus of the cerebellum, while the older nucleus magnocellularis is interposed between the cerebellar nucleus globosus and emboliformis above and the descending rubrospinal tract. He concludes that this close anatomical relationship of the nucleus magnocellularis with the cerebellum and Monakow's bundle constitutes the primitive path of nerve impulses for automatic movements. Other tracts converge on the red nucleus. Von Monakow describes a fronto-rubro-tegmental pathway. The fibres thus indicated arise in the frontal cortex and pass down via the red nucleus to the tegmentum of the mid-brain and formatio reticularis of the pons, from where they are supposed to send a relay to the spinal cord. Wilson [62] has shown that there is a considerable tract of fibres from the globus pallidus which passes across Forel's field to the anterior capsule of the red nucleus. The principal red nucleus efferents are the rubrospinal tracts of Monakow which cross the mid-line in the fountain decussation of Forel. This tract arises wholly in the giant cells, according to Cajal [10]. Von Monakow describes some fibres as coming from the cells of medium size. Certainly the tract arises chiefly from the nucleus magnocellularis, and comparative anatomical studies show that this part of the red nucleus varies directly in size with that of the tract in most animals, and both are small in man. Efferent fibres of importance also pass from the red nucleus to the tegmentum and formatio reticularis, as well as to the thalamus and frontal cortex.

Because of its venerable phylogenetic history and its wide anatomical connections, the red nucleus has been rather heavily burdened with theoretical functions. It is therefore of importance to note carefully the state of preservation of this nucleus in the experimental animals.

(c) *Results of Anatomical Examination.*[1]

Animal I.—Death on the eighteenth day after decerebration. Post-mortem performed about thirty minutes after death, immediately after removal from bath. Along the scalp incision there was an area of superficial cellulitis. No evidence of intracranial tension. A lump of wax filled the cranial cavity conforming to its outline. On removing the wax a thin layer of pus was found beneath it. The brain-stem and spinal cord were removed and placed in formol. See photographs of brain-stem, figs. 9 and 10. Incision A—B, fig. 9, corresponds to line A—C, fig. 11.

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[1] In a number of experiments the preparations died and remained in the warm bath long enough for the brain-stem to become soft. In such cases no microscopic examination was possible.

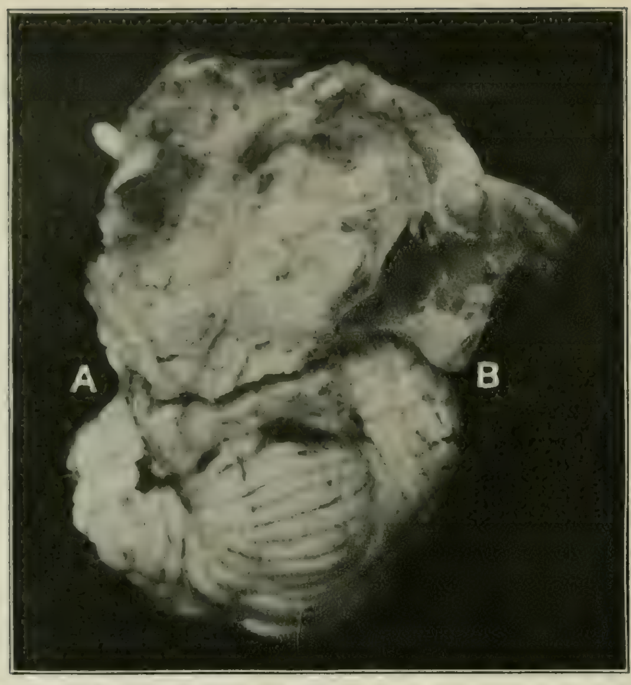

FIG. 9.—Experiment I. Photograph of brain-stem taken from above the cerebellum.

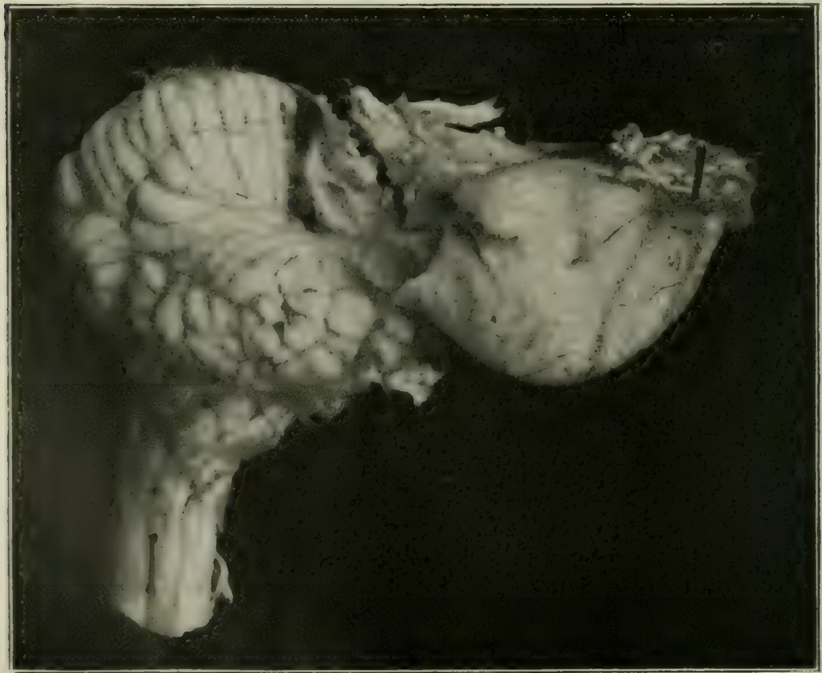

FIG. 10.—Experiment I. Lateral view of brain-stem showing the temporal pole which was not removed.

The only remaining portion of the cerebral cortex was a small part of the right temporal lobe which was attached to the brain-stem by a thin piece of nervous tissue overlying the infundibulum. Thus the pituitary and probably its blood-supply were preserved. All of the basal ganglia were removed above line A—B, fig. 11. A little below the level of the tentorium was an incision A—C, almost entirely severing the brain-stem. It began dorsally just behind the inferior colliculus and passed ventrally on a plane just caudal to the anterior end of the pons, but did not quite completely sever the cerebral peduncles. This incision had severed the right fifth nerve close to the pons.

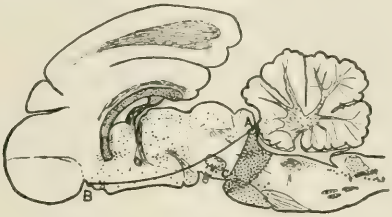

FIG. 11.—Experiment I. All of the tissue above line A—B was removed. A second incision at line A—C was almost complete as indicated. Dotted area represents extent of softening on right side.

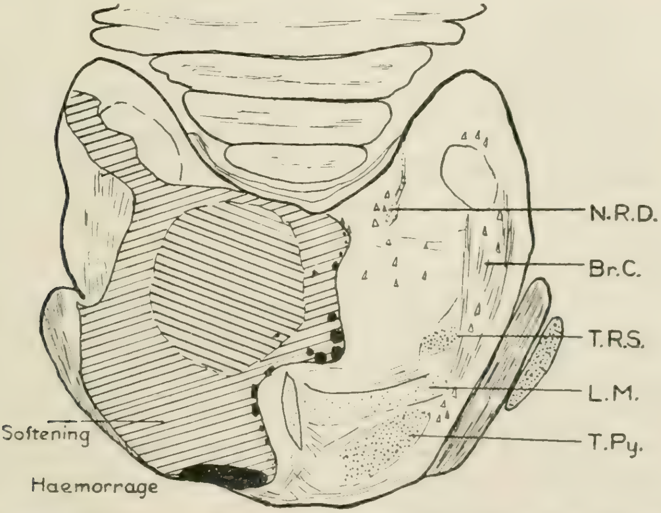

FIG. 12.—Experiment I. Drawing made with the aid of an Edinger apparatus, from a section stained by Loyez's hæmatoxylin method for the fibre tracts. The cell groups indicated by small triangles were added from the next section in the series stained by Nissl's method. The large area of softening has an outer part filled with compound granular corpuscles and an inner area which contained no cellular elements. N.R.D., nucleus of descending or mesencephalic root of V nerve; Br.C., brachium conjunctivum; T.R.S., rubro-spinal tract; L.M., medial lemniscus; T.Py., pyramidal tract.

After fixation, block I, including the tissue above and below incision A—C, and block II, just below this, were cut in series and alternate sections were mounted and stained by Nissl's method and by Loyez's hæmatoxylin method. The latter method demonstrates the tracts clearly. The rest of the central nervous system was stained by the Marchi method for degenerated fibres, and cut and mounted in series.

Microscopical examination shows that the red nuclei are present in the segment of nervous tissue above the incision A—C. All of the giant cells in both nuclei show marked chromatolysis, although the medium and small sized cells were for the most part normal. This indicates that the descending fibres of Monakow's bundle had been severed. Immediately below the incision A—C was an area of softening occupying practically the whole of the right half of the upper pons, as shown by the heavily dotted area in fig. 11, and passing across the mid-line dorsally. This area (see fig. 12) was separated by a line of hæmorrhage from the normal tissue of the left side. Even had the descending red nucleus fibres of this side not been severed by the incision A—C, they would have been destroyed in this area of softening. There was no evidence of encephalitis anywhere within the nervous tissue. The softening was evidently the result of hæmorrhage at the time of operation. If the experiment had been acute instead of chronic, it is quite possible that this area would have been passed as normal, although it was doubtless functionally inactive from the start.

The cerebellum was normal and it should be noted that although there was, of course, interruption of the tract connecting cerebellum with red nucleus and thalamus, the ventral spino-cerebellar tract of Gowers was intact and showed no degeneration. There were degenerated fibres in the middle cerebellar peduncles, as would be expected from the injury to the nuclei pontis, and there were a few degeneration granules in the restiform body. Vestibular nuclei were intact.

The Marchi sections beginning in the pons and passing downwards showed degeneration as follows. (Refer to drawings, figs. 13, 14, 15, 16, 17, 18; black dots indicate degenerated tracts.)

(1) The pyramidal tracts show rather fine degeneration-granules. It was noted that immediately below the pons degenerated fibres came off from the pyramidal tracts, decussated at once and passed outward among the fibres of the trapezoid body (fig. 14). They could not be definitely traced beyond the superior olivary nucleus and the medial trapezoid nucleus. Below the corpus trapezoidium also, the decussation of these pyramidal fibres continued. Their ultimate destination

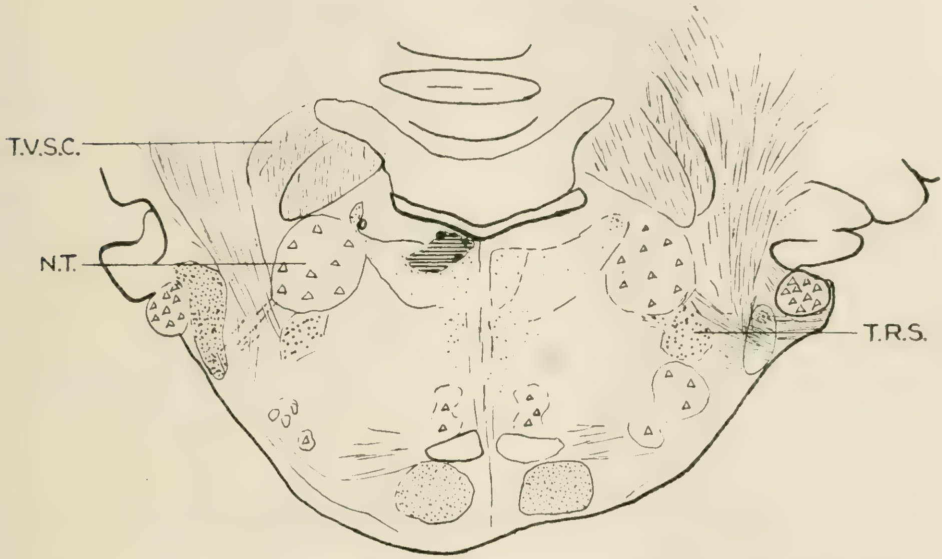

FIG. 13.—Experiment I. Section prepared by Marchi's method to show degenerated fibres. The area of softening described above (fig. 12) is represented at this level only by a small area beneath the fourth ventricle. T.R.S., rubro-spinal tract; N.T., nucleus of trigeminal nerve; T.V.S.C., ventral spino-cerebellar tract.

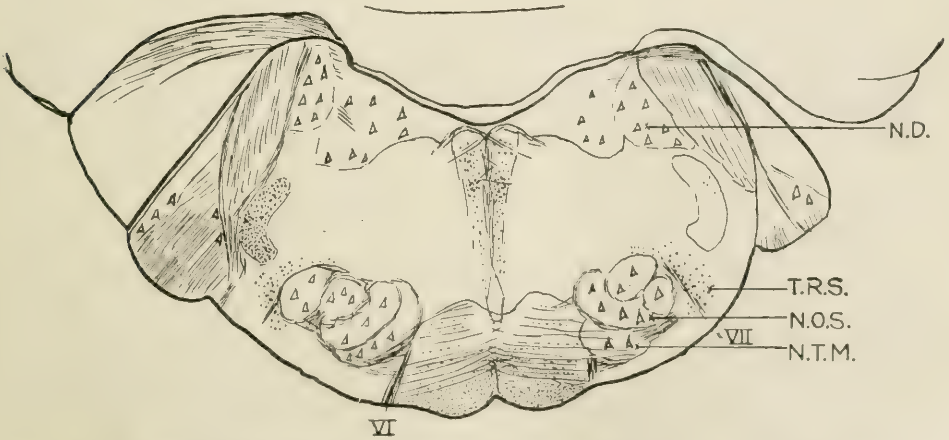

FIG. 14.—Experiment I. Marchi stain. Degenerated fibres may be seen to decussate in the mid-line and pass outward in the trapezoid body as far as the medial nucleus. N.D., Deiters' nucleus; T.R.S., rubro-spinal tract; N.O.S., nucleus of the superior olive: N.T.M., medial nucleus of the trapezoid body.

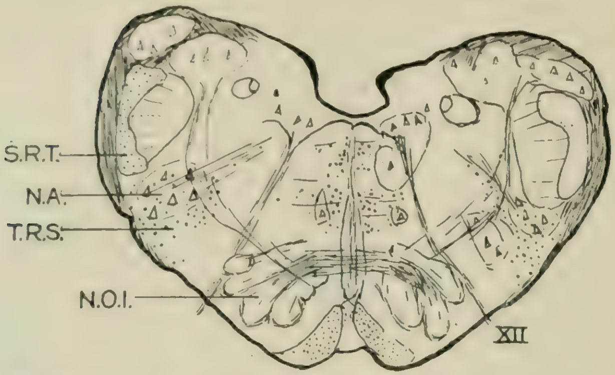

FIG. 15.—Experiment I. Marchi stain. S.R.T., sensory root of trigeminal nerve; degenerated fibres due to section of the nerve; N.A., nucleus ambiguus; T.R.S., rubro-spinal tract; N.O.I., inferior olive.

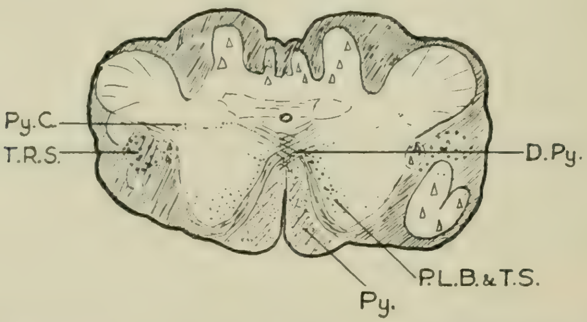

FIG. 16.—Experiment I. Marchi preparation. The degeneration granules of the decussating pyramidal fibres are finer than those of the rubro-spinal tract. It is no longer possible to distinguish tecto-spinal tract from posterior longitudinal bundle. Py., pyramidal tract; Py.C., crossed pyramidal tract; T.R.S., rubro-spinal tract; D.Py., decussation of the pyramids; P.L.B. & T.S., posterior longitudinal bundle and tecto-spinal tracts.

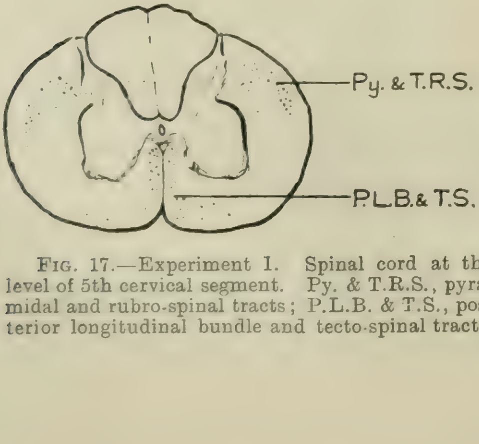

FIG. 17.—Experiment I. Spinal cord at the level of 5th cervical segment. Py. & T.R.S., pyramidal and rubro-spinal tracts; P.L.B. & T.S., posterior longitudinal bundle and tecto-spinal tracts.

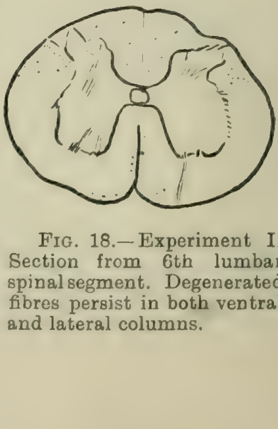

FIG. 18.—Experiment I. Section from 6th lumbar spinal segment. Degenerated fibres persist in both ventral and lateral columns.

could not be determined except that there seemed to be an increase in the number of scattered degeneration-granules in the formatio reticularis. In a personal communication Dr. Gordon Holmes has suggested that these fibres may be cortico-bulbar. Further study of this tract is projected with several other possibilities in mind.

(2) Posterior longitudinal bundle presented in the pons a sprinkling of coarse granules near the mid-line. At the top of the medulla they are displaced ventrally by the bundles of entering fibres from the vestibular system. These degenerated fibres pass downwards into the ventral columns of the spinal cord, together with the fibres of the predorsal bundle from which they cannot be distinguished.

(3) Predorsal fibres (presumably tecto-spinal) pass downward from the highest section, on either side of the raphé, only distinguishable from the degenerating fibres in the posterior longitudinal bundle by their more ventral location and their denser grouping. In the cord they are indistinguishable from the posterior longitudinal bundle fibres with which they enter the ventral columns where degeneration-granules are easily followed as far as the lower lumbar segments (figs. 17, 18).

(4) The descending motor fibres or mesencephalic root of the V-nerve were found degenerated from beneath the lateral limits of the fourth ventricle to the middle of the pons, where they turned and passed through the chief sensory nucleus of the V, just lateral to the rubrospinal tract, and joined the trunk of the V-nerve. The sensory root of the V was completely degenerated on the right, due to section of the nerve at the base of the skull, and the degenerated fibres could be followed downward in the spinal root of the V. There was also a small group of degenerated descending fibres in the spinal root of the left V-nerve.

(5) The descending fibres of the rubrospinal tract were replaced by myelin granules about equal in number on the two sides and differing from the pyramidal fibre granules by being coarser than the latter. At the level of the superior olive the rubrospinal tract has moved ventrally and laterally so as to pass in a band around the lateral boundary of the superior olivary nuclei (fig. 14). The fibres then enter the seventh nucleus, which lies immediately below, and are sprinkled out among the cells of this nucleus and its caudal continuation, the nucleus ambiguus (fig. 15). A few of the degenerated fibres pass dorsalwards with the fibres of the seventh nerve-root toward the genu of that nerve, and likewise at a lower level with the dorsally

directed motor fibres of the ninth and tenth nerves from the nucleus ambiguus (fig. 15). The degenerated tract was traced directly down to its characteristic prepyramidal position in the cord.

To summarize the anatomical findings in Experiment 1: There was a small amount of pus about the wax in the cranial cavity. There was, however, no encephalitis of the brain-stem. That the red nuclei did not function after the operation is shown as follows: (1) There was chromatolysis of the caudal end of each red nucleus—the nucleus magnocellularis. (2) The incision A—C appeared microscopically to have cut across Monakow's bundle. (3) The area of hæmorrhagic softening which destroyed the whole of the right side of the brain-stem in the upper pons likewise destroyed the rubrospinal tract on that side (fig. 12). (4) There is a heavy degeneration of the rubro-medullary and rubrospinal tracts, shown by Marchi's method, about equal on the two sides. It is possible to state with certainty, therefore, that all of the mesencephalon and higher centres were removed or without connection with the rest of the organism, except that the hypophysis and its blood supply were intact. The metencephalon, except for the area of hæmorrhagic softening in the upper pons, was intact, and its neurones capable of functioning, as demonstrated by Nissl stains.

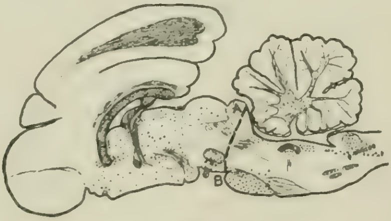

FIG. 19.—Experiment XXI.

Animal XXI (p. 221).—Death on the twenty-second day after decerebration. Cause of death, pneumonia, and intracranial infection. The decerebration was complete. All of the cerebrum and basal ganglia were removed, the line of decerebration passing through the middle of the inferior colliculus dorsally to 1 mm. above the upper edge of the pons ventrally. (Line A—B, fig. 19). Brain-stem and segments of cord were stained by the Marchi method. There was degeneration of the corticospinal, rubrospinal, and tectospinal tracts, and the posterior longitudinal bundle. Degenerated fibres were traced into the lowest dorsal segments in the ventral and lateral columns.

Animal II (p. 195).—Death on the twenty-third day after decerebration. Cause of death, accident due to lively running movements. Lungs showed evidence of recent broncho-pneumonia in recovery stage. The level of decerebration was more anterior than in the last one described, passing between the superior and inferior colliculi dorsally. The section was slightly oblique, removing more tissue on the left than on the right. No note was made of the level ventrally, but Marchi sections of the brain-stem and cord showed heavy bilateral degeneration of the rubrospinal tract in addition to degeneration of the other descending tracts (see fig. 20). Therefore, most, if not all, of the red nucleus must have been removed. Degenerated tracts were followed down into the lower lumbar segments in the lateral and ventral columns.

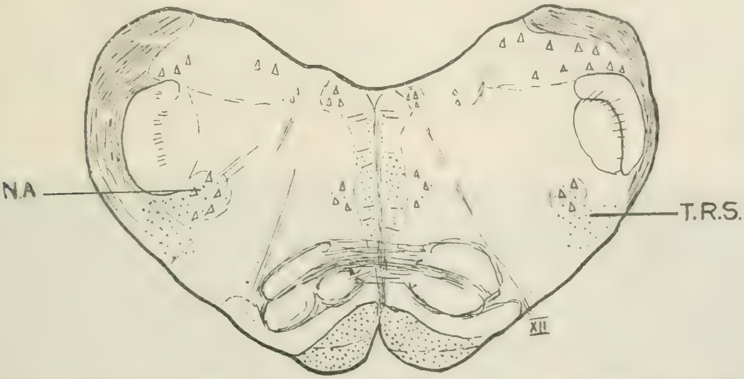

FIG. 20.—Experiment II. Marchi preparation. T.R.S., rubro-spinal tract; N.A., nucleus ambiguus.

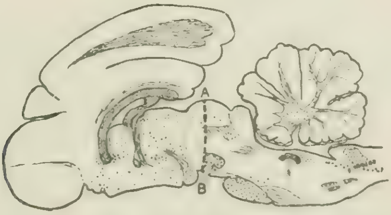

FIG. 21.—Experiment IX.

Animal IX (p. 203).—Death on the eleventh day after decerebration. Infected hæmatoma beneath wax. The level passed through the superior colliculus dorsally and just in front of the emerging fibres of the third nerve ventrally (line A—B, fig. 21). The time was not sufficient to provide for complete degeneration, but there were a few black granules shown by the Marchi method in the pyramidal tract and posterior longitudinal bundle, and also the rubrospinal tract. One may assume, therefore, that there was some injury to the red nuclei, unless some of the fibres of Monakow's bundle have a higher origin, e.g., thalamus, as claimed by Bechterew [5].

Animal XVII (p. 218).—Death nine days after decerebration. The level was between the superior and inferior colliculi dorsally. No note was made of the ventral level but some of the hippocampus was left on the right side. Microscopic examination by the Marchi method showed degeneration in all the chief descending tracts, including the rubrospinal. The reaction of degeneration was incomplete, doubtless due to the short time which had elapsed since decerebration.

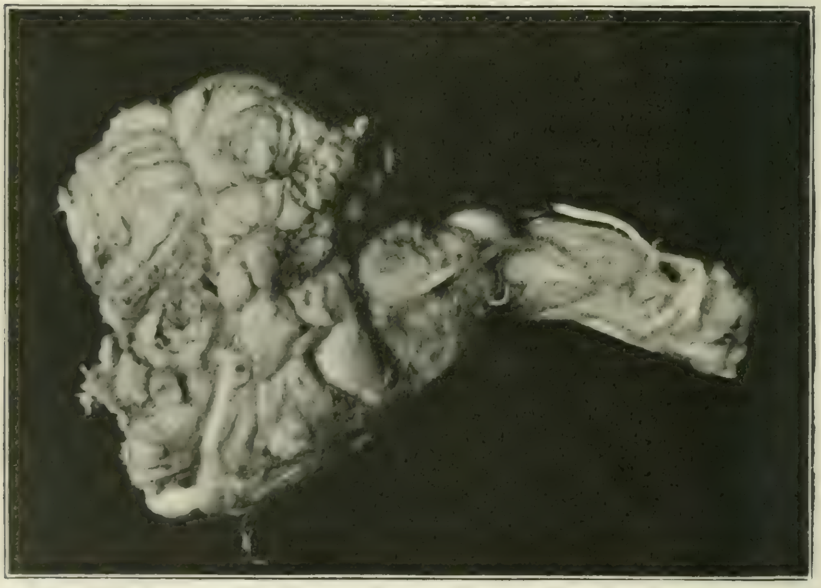

FIG. 22.—Experiment XXIII. The under-surface of the remaining mesencephalon may be seen above the upper margin of the pons.

Animal XXIII (p. 222).—Death five and a half days after decerebration. There was hæmatoma beneath the wax in the cranial cavity. The lungs were congested and there was exudate in the bronchi. The decerebration had been complete. All of the colliculi had been removed and some of the tegmentum caudal to the inferior colliculus. Ventrally, the level of incision was considerably higher, leaving 4 mm. of the left cerebral peduncle above the pons, and 2 mm. of the right. See photograph of the brain-stem, taken from the left side (fig. 22), also schematic representation of the level (fig. 23). Microscopical sections were made of the top segments, by the Nissl and Loyez methods. There was no encephalitis. The red nuclei were present, at least in part, and may have been functioning.

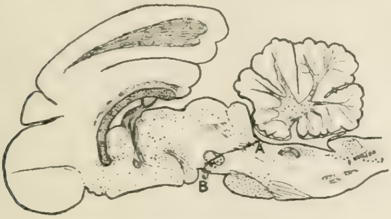

FIG. 23.—Experiment XXIII.

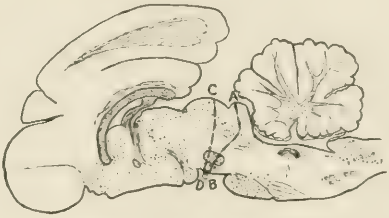

FIG. 24.—Experiment XXVI.

Animal XXVI (p. 226).—Death three days after decerebration. No cause of death could be ascertained. The decerebration was oblique, the level indicated in fig. 24 by the line A—B for the left side and the line C—D on the right side. Microscopical examination of sections through the top block of the brain-stem showed more of the red nucleus present on the right than the left. Most of the cells of the nucleus magnocellularis showed chromatolysis. The right inferior colliculus was intact. Part of the left inferior colliculus was missing.

Animal VI (p. 201).—Death two days after decerebration. No cause of death determined. The microscopical level of decerebration, which was oblique, is shown in fig. 25, by the line A—B for the left side and C—D for the right side. Microscopical sections showed a circumscribed area of hæmorrhage which destroyed most of the left red nucleus and probably all. The cells of the right red nucleus were present. About half of the large cells showed chromatolysis, the rest were normal. There was no infection. Both inferior colliculi were normal and there was no interference with the lateral fillets.

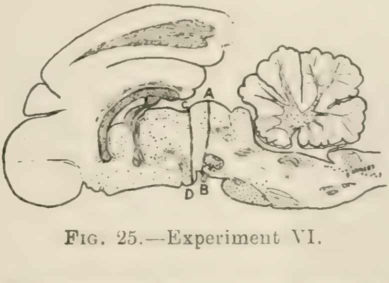

FIG. 25.—Experiment VI.

Animal IV (p. 199).—Killed on the sixth day after decerebration. There was evidence of beginning broncho-pneumonia. The decerebration was complete except for a piece of the left crus, which was attached to the pons by a narrow strip of tissue. The pituitary was intact with its blood supply. The macroscopical level of decerebration is shown by line A—B. fig. 26. Microscopically the whole top of the brain-stem was softened and infected, except the narrow strip of pyramidal fibres where the piece of cerebral peduncle mentioned above was attached. There was an area of hæmorrhage in the right proximal half of the pons, destroying the formatio reticularis here. There was no encephalitis in the deeper segments of the pons. The cells of the vestibular nuclei and the nuclei of Deiters were for the most part normal, but large cells in the formatio reticularis (called nucleus salivarius superioris by Winkler and Potter[64] all showed chromatolysis, suggesting that their axones had been sectioned. There was no evidence of red nucleus anywhere.

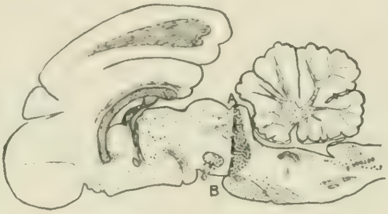

FIG. 26.—Experiment IV.

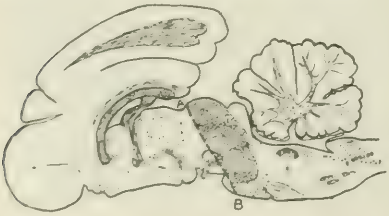

FIG. 27.—Experiment V. Left side.

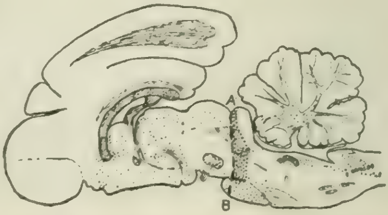

FIG. 28.—Experiment V. Right side.

Animal V (p. 200).—Killed in apparently good condition on the sixth day after decerebration. There was ophthalmia of the right eye and the right V nerve was damaged near its exit from the pons. The level of decerebration as seen microscopically passed through the superior colliculus on the left side (A—B, fig. 27), and between the two colliculi on the right side (A—B, fig. 28).

Ventrally it came below the upper margin of the pons, but there was a small block of tissue attached by some of the fibres of the crura cerebri to the pons. This overlay the pituitary whose blood supply was apparently intact. There was a considerable hæmorrhage extending down into the pons and causing destruction of almost all the normal tissue indicated in the dotted areas of figs. 27 and 28. There was cuffing of the vessels with polymorphs showing that there was some encephalitis of the superficial areas in addition to the softening due to hæmorrhage. Such of the decussation of Meynert and Forel as may have existed was completely destroyed. Careful microscopical examination showed the red nuclei removed or destroyed by hæmorrhage. On the left side the formatio reticularis was destroyed at least as far down as the middle of the pons. On the right a few nerve cells could still be recognized in parts of the upper pons, but they were not normal as shown by Nissl staining. The destruction did not reach as far as Deiters' nucleus.

In this case it is certain that the red nucleus on both sides was completely destroyed. Much of the inferior colliculi was left and microscopically normal, but all connection of these centres with the rest of the brain-stem was severed. The level of decerebration is in reality the middle of the pons.

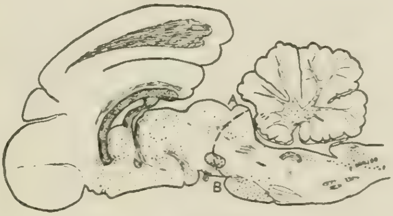

Fig. 29.—Experiment VII.

Animal VII (p. 202).—Death twenty-eight hours after decerebration, due to hyperpyrexia after warming before stove. No evidence of infection. A small amount of isolated brain tissue remained over the infundibulum. Top of brain-stem was smooth, symmetrical, and convex in outline, beginning in the middle of the inferior colliculi dorsally and the upper border of the pons ventrally. (Fig. 29, line A—B).

To microscopical examination, part of the red nucleus was present on either side and many of the cells were normal. Several small areas of hæmorrhage extended downward a few millimetres. The pons was otherwise normal.

Animal VIII (p. 203).—Death on the seventh day after decerebration due apparently to secondary hæmorrhage from the brain-stem. There was pus and blood-clot between the wax and the brain-stem. Progressive microscopical sections showed that there was no encephalitis below the superficial layers. To microscopic examination the level of decerebration passed between the superior and inferior colliculi on the right and through the middle of the inferior colliculus on the left, to end at the upper border of the pons ventrally. See figs. 30 and 31. A small amount of brain matter remained above the infundibulum. The tissue corresponding to the dotted areas was softened and filled with compound granular corpuscles.

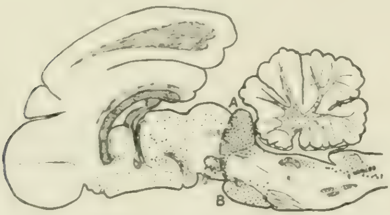

FIG. 30.—Experiment VIII. Right side.

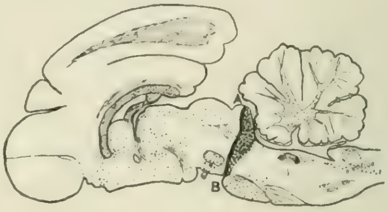

FIG. 31.—Experiment VIII. Left side.

There was no remnant of red nucleus on the left side and only a few cells belonging to this nucleus remained on the other side. The interpeduncular ganglion and most of the substantia nigra cells were normal as well as the pontile nuclei. Most of the formatio reticularis was normal. With the exception of a small proportion of the cells of the right red nucleus, the level of decerebration was below the mesencephalon.

CHAPTER VI.

(a) *Decerebrate Rigidity in Chronic Experiments.*

Decerebrate rigidity was first mentioned in experimental animals by Sherrington in 1896 [53]. He described it as a "tonic rigidity in certain groups of skeletal muscles, especially those in the dorsal aspect of the neck, tail, and of the extensor surfaces of the limbs." Decerebrate rigidity in animals is, then, a tonic rigidity of the anti-gravity muscles, the muscles employed in maintaining an erect posture.

The neurogenic source of this phenomenon has been the subject of many studies. Hughlings Jackson [24] had suggested that the cause of hemiplegic rigidity in clinical cases was due to the "unantagonized influence of the cerebellum" . . . "after the influence of the cerebrum is taken off." Similarly, the decerebrate rigidity of experimental animals has been commonly considered a release phenomenon.

It has been maintained that the red nuclei were the source of the rigidity after decerebration through the mid-brain or after a lesion to the cerebellum. The intimate connection of these twin nuclei with cerebellum, thalamus, globus pallidus, and spinal cord seems to fit it for such a function. Moreover, it has been shown, notably by Graham Brown [9], that electrical stimulation of the red nuclei results in a postural response and the stimulation is followed by a well maintained after-discharge. In a different way, Magnus and his co-workers have demonstrated these postural movements also. They have described a number of position reflexes which may be seen in the decerebrate animal. Many of these position reflexes take place only if the mid-brain including the red nucleus be present. Others continue to be seen after the removal of the mid-brain. But because mid-brain and red nucleus may have to do with position mechanisms, as indicated above, it does not necessarily mean that they are indispensable for the maintenance of extensor rigidity.

The experiments reported in this paper prove that the red nuclei are *not* necessary for the maintenance of decerebrate rigidity. Inasmuch as the animals were kept for long periods of time the possibility of irritation effects disappears. The rigidity must be a release phenomenon. But it is not release of the rubrospinal tract.

Careful microscopical examination, as described above, showed for example that in experiments IV and V there was no red nucleus to be found. In experiment I, cells of the red nucleus were found in a block of tissue which was severed from the brain-stem. Below this the area through which the rubrospinal tract must have passed was completely softened and below this there was heavy degeneration of the rubrospinal tracts. In other experiments (as II, VIII, XVII, XXVI) the greater part of the red nuclei was missing and probably the remnant was not functionally active.

In experiment I, just mentioned, the animal showed extensor rigidity during the early days following operation, and at times this rigidity was seen to vary in intensity during an examination. On the twelfth day after operation it was noted that the right hind-leg was rigid in flexion while the other limbs maintained extensor rigidity. In experiment IV there was extensor rigidity of moderate intensity on the first two days after operation. During the next two days a tendency was noted to assume a rigidly flexed attitude. On removal from the bath to be dried, extreme extensor rigidity appeared with retraction of the head. This was followed by a short period of tonic flexion of the limbs and extrusion of the fore-claws. There were then several alternations of flexor and extensor rigidity.

Animal V developed extensor rigidity on the day of operation. Next day it was much increased. On the third day the extensor rigidity was marked, especially after the animal had been handled and turned in the bath. The tone was probably sufficient to support the weight of the body with ease. On the sixth day the animal was removed from the bath and dried in the incubator. During the drying process there was no rigidity, the limbs being flaccid. After this one of the nerves was dissected out for a stimulation experiment. During the dissection there were vigorous movements, micturition and the development of extreme extensor rigidity which was maintained during manipulation, but lessened when the animal was left quiet for a quarter of an hour. During further dissection extreme rigidity returned. By reference to p. 251 it will be seen that because of softening, the actual level of decerebration in this animal was the middle of the pons. Preparation VIII developed a considerable extensor rigidity in all four limbs immediately after operation. On the fourth day extreme rigidity was noted in all four limbs, but after the preparation was turned from the right to the left side the right fore-limb went into tonic flexion with extrusion of claws. Many of the position reflexes described by Magnus were later elicited in this preparation. (See p. 203.)

It is unnecessary to multiply examples. Decerebrate rigidity appears even though the red nuclei be removed. The preparations with high decerebrations acted differently, went into violent running movements, and were much more difficult to keep alive than those in which the removal was more posterior. There was perhaps more variability in the posterior removals, and the rigidity is frequently intensified by afferent stimuli. This variability was noted by Cobb, Bailey, and Holtz [11] in acute preparations, as well as the effect of afferent stimulation. Magnus [40] concluded that to remove the midbrain resulted in the loss of the ability to bring the body to normal from any abnormal position. The difference in the behaviour of the preparation according to the level of decerebration cannot be denied. Whether or not there is any difference between the rigidity of the animals with and those without red nucleus, as suggested by Cobb, Bailey and Holtz, must be decided by myographic examination of the tonus of isolated muscles. To less refined methods of examination the rigidity when present is the same regardless of the fate of the red nuclei.

In a number of the complete decerebration experiments, retraction of the head amounting to opisthotonos appeared in preparations which at the same time showed extreme extensor rigidity and this was frequently spasmodic. That is, head retraction appeared periodically together with an increase in extensor rigidity. It seems that when extensor rigidity becomes sufficiently intense, opisthotonos usually appears as a part of the same phenomenon, as Wilson [63] has suggested for tonic fits in man.

The term decerebrate rigidity is generally taken to mean extensor rigidity. But in completely decerebrated specimens another type of rigidity sometimes appears, tonic contraction of the muscles on the *flexor* aspect of the limbs. This is associated at times with bending of the head downward and extrusion of the fore-claws. After *semi*-decerebration this phenomenon appeared much more frequently (p. 232), alternating with extensor rigidity as though complementary to it. It would be more accurate, therefore, to speak of extensor and flexor rigidity as two types of decerebrate rigidity. Sherrington, Thiele, and Weed have independently noted the occasional appearance of flexor rigidity.

Study of the results of the more anterior unilateral decerebrations demonstrates that the extensor rigidity may be ipsilateral in the acute preparation, as described by Sherrington, but that after the stage of stimulation disappears the extensor rigidity becomes contralateral in the chronic preparation. Correspondingly, flexor rigidity, though sometimes contralateral at first, quickly becomes ipsilateral. These observations suggest that the fibres whose interruption give rise to extensor rigidity decussate somewhere between the anterior part of the mesencephalon and the upper part of medulla oblongata. This is in agreement with the experiments of Thiele.

The anatomical basis generally accepted for extensor rigidity at present is, very briefly : the rigidity is a proprioceptive reflex depending on the integrity of the local reflex arc, including the afferent and efferent paths to any muscle in question (Sherrington) [56]. The condition appears only after section of the brain as low as the posterior part of the thalamus (Thiele) [57], or the anterior part of the mid-brain (Magnus) [40]. In the chronic experiments of de Barenne there was no rigidity after removing fore-brain, leaving thalamus intact. It would seem that the tract whose interruption is responsible for decerebrate rigidity has its origin about the level of the hypothalamus.

On the other hand, section of the brain-stem below the pons immediately abolishes the rigidity on the ipsilateral side [54], but not on the contralateral side. The phenomenon is therefore independent of the pyramidal tract. The nerve paths responsible for the decerebrate rigidity, whatever their source may be, are found in the anterolateral columns of the cord, since cutting the posterior or the ventral columns does not influence rigidity.

There has been considerable discussion as to what is the source of the tonic influence which is brought into play by decerebration. It must be located in the pons or upper medulla oblongata. The action of this centre, or perhaps reflex arc, is modified by stimuli from the otic labyrinth although decerebrate rigidity is not abolished by section of the eighth nerve [54]. There exists an area on the anterior surface of the vermis cerebelli, stimulation of which inhibits decerebrate rigidity [53], [33], [59], [11]. Removal of this area induces this condition if not already present. Rigidity has been observed to continue for some time after total ablation of the cerebellum. Cobb, Baily and Holtz [11] maintain that the inhibitory pathway is the dentate-rubral fibres. Weed believed the cerebellum to play an important rôle in the cause of decerebrate rigidity, but the removal of the cerebellum in his experiments did not abolish it immediately. Thiele [57] reported that progressive removal of slices of the cerebellum induced decerebrate rigidity until the vicinity of Deiters' nucleus was reached, when all rigidity suddenly disappeared. This author likewise made progressive sections down the brain-stem and reported that the decerebrate rigidity which appeared when the section passed below the posterior end of the thalamus, disappeared suddenly on reaching the level of Deiters' nucleus. These were acute not chronic experiments. Magnus considers that the decerebration must be as low as the anterior part of the mid-brain before rigidity results. He describes decerebrate rigidity as a caricature of standing, inasmuch as the ability to assume and maintain an upright position disappeared with the removal of the mid-brain [40]. Magnus likewise agrees that decerebrate rigidity may persist until the level of removal reaches the lower margin of the pons.

It has been shown that the mid-brain and pons of a decerebrate preparation can be bisected in the sagittal plane without loss of decerebrate rigidity. On one occasion we confirmed this, as follows:—

A complete decerebration was performed on a cat at 11 o'clock in the morning. The level was between the colliculi dorsally and 3 mm. in front of of the anterior margin of the pons ventrally. The extensor rigidity was well maintained and the preparation would stand if properly adjusted on its feet. At 4.45 p.m. a sagittal mid-line incision was made through mid-brain, pons and well down into medulla oblongata. The rigidity continued and was still in evidence at 6.15 p.m. By this time the rigidity was less intense and the respiration was just coming to a stop. The lungs were artificially ventilated. The limbs, after a stage of clonus, improved their extensor rigidity for a time.

Examination of the brain-stem showed the longitudinal section to be complete at the level of the red nuclei. At the level of the upper medulla the the bisection was complete dorsally but stopped 1 or 2 mm. short of the ventral surface, only severing a part of the inter-olivary body. In the lower medulla a considerable hæmorrhage had occurred which may have been responsible for the respiratory failure.

As the rubrospinal tract decussates almost completely in the midline, this is added evidence that the presence of the red nuclei is not essential to the existence of decerebrate rigidity. The experiment likewise suggests that paths which are responsible for decerebrate rigidity do not decussate in the medulla.

Nothing has been encountered in these experiments which would contradict the view of Thiele that the integrity of Deiters' nucleus is essential for the production of decerebrate rigidity, or that the spinal fibres arising in Deiters' nucleus carry efferent impulses indispensable to the reflex. Weed suggests that the ventral cerebellar tract of Gowers carries afferent impulses in the reflex circuit, which is responsible for the rigidity. This tract passes dorsally below the level of even the lower decerebrations and was seen to be intact in all of our anatomical preparations that were carefully studied.

(*b*) *Temperature Control.*

The whole literature on the subject of temperature control and the nervous mechanisms which are concerned has been so carefully reviewed recently by Barbour [1] that no attempt need be made here to give any detailed account, and reference may only be made briefly to such papers as bear most closely on the results here reported.

It has been shown by Rogers [50] that in pigeons section of the brain-stem below the level of the thalamus completely removes all temperature control, while section above the thalamus does not, so that even in birds, in which the development of the corpus striatum is very different from that of mammals, section of the brain-stem in the region we have studied destroys all temperature control. The similarity with the results obtained in cats is the more marked when the experiments of de Barenne [2] [7] are also taken into consideration. He removed practically all the brain above the thalamus in the second of the two cats described in the above paper, and yet found it to have a normal temperature control. Therefore, in cats also the control of temperature may be definitely located between the level of the middle of the superior colliculi and 2 mm. in front of the pons below and the upper limit of the thalamus above. Such a situation for the centres controlling temperature regulation is in entire accord with the work of Barbour on the effect of localized heating of the brain.

Isenschmidt and Krehl [22] in 1912 showed that rabbits in which the brain-stem was divided at the level of the junction of the diencephalon and mesencephalon lost all power of temperature control, while if the hemispheres alone were removed control was not lost. But their animals without temperature control only survived a few days, and considering how long reactions may be depressed following a lesion, the possibility of a later return of temperature control was not excluded.

Later Isenschmidt and Schnitzler [23] made various sections in the mid-brain at different levels, these sections being often one-sided and partial, and they came to the conclusion that the heat regulation centre was in the region of the tuber cinereum. This would be consistent with our results, but their conclusions cannot be regarded as firmly established since again they were unable to keep alive for more than a few days any animals which lost their power of temperature control. Consequently they could not elaborate their results by examination for nerve degeneration. The "Zwischenhirnstich" of Leschke [31] gave similar results.

The animals that we report offer therefore strong confirmatory evidence as to the position of the centres controlling temperature, and it should be much easier to determine whether these are in the thalamus or tuber cinereum by the employment of the methods we have developed for nursing animals which have lost their power of temperature regulation.

It will be evident from the experiments that have been described that no sign of temperature control remains and that no such control returns at any rate within two weeks. The complete absence of shivering in the bilaterally operated animals and its ready occurrence after the unilateral operation is very striking, and it is of considerable interest that in the latter case shivering occurs equally on the two sides of the body. With the unilateral decerebrations it was noticed that if the remaining brain matter was exposed to some pressure (as occurred when wax was used in these cases) the raised intracranial pressure readily destroyed the power of temperature control, and it was also noticed that in the other animals which showed deficiency of temperature control the lesion had slightly damaged the left side of the brain-stem as well as the right.

It seems probable, therefore, that tracts which carry either sensory or motor fibres intimately concerned in temperature control run in the mid-brain close to the mid-line, possibly for instance in the posterior longitudinal bundle, though we have no direct evidence of this.

The animals with bilateral decerebration showed a considerable change in the respiratory rate with change in body temperature in spite of the apparent absence of temperature control. This however appears to be adequately explained by assuming that a rise in body temperature alters the respiratory rate by affecting the respiratory centre directly, just as it alters the heart rate by direct action on the heart, and that the respiratory rate may be still further quickened by the indirect action of a metabolism which has also been increased as the result of the raised body temperature. In any case the quickening of the respiratory rate with raised body temperature is probably considerably less than that occurring in the intact animal [20] [30] [48].

While up to the present these preparations have given no great additions to our knowledge of the mechanisms concerned in temperature control, the possibility of the preservation over long periods of animals, in which this control has been lost, would seem to offer many new opportunities for the investigation of this problem.

Conclusions.

(1) A technique is described which allows cats in which all the brain above the level of the pons has been completely removed to be preserved for days and occasionally as long as three weeks. The essential factor is shown to be the maintenance artificially of a normal body temperature.

(2) Chronic decerebrate preparations obtained in this way are found to maintain throughout this period the general characteristics described by Sherrington. The extensor rigidity is usually maintained with brief intermissions, and further proof is thus offered that it is a "release phenomenon." Rigidity continues in many cases after full degeneration of the divided tracts has occurred.

(3) Decerebrate rigidity is described lasting for more than two weeks in animals in which all the red nuclei can be shown histologically to be no longer functioning. Decerebrate rigidity can therefore occur in the absence of the red nucleus, and although many reactions and position-reflexes disappear in the more posterior decerebrations, the character of the extensor rigidity seems to be the same. It was

sometimes found that sensory stimuli would increase the rigidity already present, or cause it to reappear if it were absent.

(4) Decerebrate rigidity is probably dependent on some centre or reflex arc at about the level of Deiters' nucleus. None of our histological examinations showed any lesion to this nucleus nor to the ventral spino-cerebellar tract of Gowers, and the rigidity did not disappear after mid-line sagittal section of the pons and medulla.

(5) Head retraction accompanies extreme rigidity, but is only seen with other evidences of an irritative lesion such as may be produced by progressive hæmorrhage. It then forms a part of what may be called a tonic extensor fit which on the day of operation occasionally developed into a well marked opisthotonos. Spontaneous nystagmus sometimes appears also as the result of this irritation.

(6) The level of the section was generally rather oblique and usually more was removed on the left side; many animals showed an asymmetric head position, usually with a tendency to bend it to the left side. In these animals the section level suggested a possibility of some of the right red nucleus cells still functioning.

(7) Certain differences between the acute and chronic states were noticed. In the later stages there is a much greater tendency for flexed positions to be assumed, and these are often asymmetrical and sometimes flaccid and sometimes rigid. Of these rigid flexion of the terminal joints of the fore-limbs with extrusion of the claws is very common.

(8) The preparations show no sign of temperature control and never shiver. Bilateral shivering is however seen after unilateral decerebration where temperature regulation is preserved. Variations in the respiratory rate are seen after bilateral decerebration as the result of differences in body temperature, but these variations are probably not so great as in the intact animal.

(9) The respiratory rate is usually that normal for a cat, i.e., about 24. Normal respirations have been observed for days even when the section was at the lower margin of the inferior colliculi.

(10) Pseudaffective reflexes were usually much more developed after the first few days than immediately after operation, and new responses were seen. Besides those described in the succeeding section, movements of the head away from certain nocuous stimuli were noticed and occasionally a movement of the fore-limbs as though directed to the protection of the head.

(11) Vocalization was noted in ten of the 124 complete decerebra-

tions. This was rarely seen except after three or four days, and consisted most commonly in purring after the stomach had been filled with milk by a stomach tube. When purring was observed the animal was a kitten or a young female. Other cats growled, such sounds being never repeated, and in this case the sounds were only observed in old males. A true mew has only been observed in one animal which made such a sound on two occasions, but would not do so in response to nocuous stimuli. An ill co-ordinated cry, resembling the sound a cat may make while anæsthetized, has been observed in five animals, but it too is apparently sporadic and is rarely repeated.

(12) Many preparations show a well developed mastication reflex with chewing of the food (or tube), swallowing of the bolus and with a final nose and mouth-licking reflex. This may be initiated by mere opening of the mouth sometimes or by insertion of food into the back of the mouth. A stomach tube is merely swallowed during the first day, is often also chewed later, while after four or five days food may be well swallowed while a stomach tube is received with apparent objection, the head being moved about and attempts being made to spit it out.

(13) Movements are seen in animals with a section between the superior and inferior colliculi and these increase after the first few days. They consist of movements as described under (10) and (14), and also of spontaneous progression movements and of kicking when touched. They were distinct from the violent movement found with more anterior sections (already described by others). It has not so far proved possible to preserve animals for any time when the section has been at the level of the anterior border of superior colliculi, owing to the complications introduced by these violent reactions.

(14) Acoustic reflexes become more brisk after the first few days. Lifting of the head to one side (usually the left) has been often seen, and would sometimes occur in reaction to such slight sounds as were made for instance by entering the room quietly, and this in spite of the fact that the bath stirrer was maintaining a constant noise. Though the constant noise gave no reaction, it caused a reaction when the motor was started after a quiet interval.

(15) Glycosuria persisting for some time after decerebration (as described by J. Mellanby) is confirmed, but this glycosuria disappears again on the second or third day and does not reappear. The cessation of glycosuria is not caused by disappearance of glycogen.

(16) Unilateral decerebration was carried out on a series of seventeen

cats, the removal extending back to the level of the pons in some, to the anterior part of the mid-brain in others.

(17) In these semi-decerebrate animals forced movements were always directed away from the side of removal. The head was rotated with occiput away from the side of removal and the neck flexed and retracted so as to carry the head over to the sound side. In some of the more anterior removals a transient stage of forced movements to the ipsilateral side followed operation, to be succeeded invariably by the opposite.

(18) In experiments in which the semi-decerebration passed through the anterior part of the mesencephalon, extensor rigidity was found in the contralateral limbs. This was preceded sometimes by ipsilateral or bilateral extensor rigidity. When the semi-decerebration was more posterior and passed between mid-brain and pons, there was considerable variation in the rigidities and a tendency for them to be asymmetrical. The anatomical deduction is that the pathway whose interruption is responsible for extensor rigidity decussates in the mid-brain.

(19) A condition of increased resistance of the flexor muscles to passive extension was described, both in complete decerebrations and semi-decerebrations. In the latter, when the removal was anterior, this flexor rigidity appeared usually in the ipsilateral limbs, though it might be seen in the contralateral limbs for a short time after operation. Thus it alternated with extensor rigidity.

(20) Flexor rigidity as an entity may be described as tonic innervation of those muscles which are subjected to tonic inhibition during extensor rigidity. It is possible to speak of two types of decerebrate rigidity.

In conclusion we would express our thanks to Professor Sherrington for his continued help and advice throughout the course of the experiments, and to Dr. J. G. Greenfield for the hospitality extended to us in his pathological laboratory at Queen Square.

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THE PATHOGENESIS OF SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD, WITH SPECIAL REFERENCE TO ITS CONNECTION WITH ADDISON'S (PERNICIOUS) ANÆMIA, ACHLORHYDRIA AND INTESTINAL INFECTION.

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Subacute combined degeneration of the spinal cord has in the past been chiefly investigated by neurologists, who were only interested in a minor degree in the associated anæmia. On the other hand, the spinal changes observed in Addison's anæmia have been investigated chiefly by physicians, whose interest was in the anæmia rather than the spinal disease. The present paper is an attempt to discuss the two groups of cases from a common standpoint, and to show that both depend upon the same underlying pathological processes—oral sepsis, absence of free hydrochloric acid from the stomach contents throughout digestion, and consequent intestinal infection and intoxication.

The term Addison's anæmia is used in this paper instead of pernicious anæmia. Addison [1] first described the disease in 1847 and called it "idiopathic anæmia." Twenty years later Biermer published his work on the same subject and called the disease "pernicious anæmia." But beyond the pernicious name he invented, Biermer added little but confusion to our knowledge of the subject, and as the disease is neither idiopathic nor necessarily pernicious, there can be no doubt that "Addison's anæmia" is the most satisfactory name.

I.—The Pathogenesis of Addison's Anæmia and Achlorhydria.

Before considering the pathogenesis of subacute combined degeneration of the spinal cord, it is necessary to summarize the views we hold as a result of recent investigations on Addison's anæmia, particularly with regard to its association with achlorhydria. For the following reasons we believe that the achlorhydria is an essential predisposing cause of the anæmia.

(1) There is abundant evidence that the achlorhydria precedes the development of the anæmia. As Robert Hutchison first pointed out in 1900, there is generally a more or less long history of digestive disturbances, of the type commonly associated with achlorhydria, preceding the first symptoms of anæmia. In one case achlorhydria was actually discovered twelve, in another ten, in another three years, and in another one year before the onset of anæmia.

(2) In sixty-four out of sixty-six fractional test meals carried out at Guy's and the London Hospitals on cases of Addison's anæmia complete achlorhydria occurred throughout the period of digestion. At whatever stage in the development of the anæmia the examination is made achlorhydria is found. It was present, for example, in cases in which the hæmoglobin percentage had not fallen below 85, 85, 80 and 68; it is thus a far more constant symptom than any other, even than the hæmatological signs, such as a high colour index and the presence of megaloblasts, as these are often absent in the early stages and even temporarily when the anæmia is severe.

(3) It persists when the anæmia has almost disappeared, either spontaneously or as a result of treatment. Thus in four cases it was still present when the hæmoglobin percentage was 85, 82, 80 and 70 respectively, compared with 45, 38, 23 and 53 respectively some months or years before.

(4) There is no constant change in the curve of secretion in any form of anæmia, except Addison's. Thus fractional test meals in our last four patients with gastric or duodenal ulcer, complicated by severe secondary anæmia due to hæmorrhage, gave curves of exactly the same form as would have been expected in the absence of hæmorrhage; the percentage of hæmoglobin in these cases was 30, 33, 48 and 49, which is quite as low as one would expect to find in an average series of cases of Addison's anæmia when first examined. In two cases of secondary anæmia caused by rectal hæmorrhage with a hæmoglobin percentage of 44 and 42 respectively, and in two cases of chlorosis with a percentage of 25 and 48, the curves of gastric secretion were normal. It is obvious, therefore, that anæmia does not cause achlorhydria.

(5) In a long series of cases it becomes clear that the achlorhydria is not specific, but that whatever its origin may be, it predisposes to the development of Addison's anæmia. Bennett and Ryle [5] have shown that about 4 per cent. of normal young men have achlorhydria. The history

in many cases of Addison's anæmia points to the achlorhydria being of this congenital type. In one it was due to alcoholic gastritis, in another it resulted from a gastro-enterostomy for ulcer, and—what proves conclusively that it is primary and not secondary—in at least five cases Addison's anæmia followed the artificial achylia produced by total gastrectomy performed for cancer. There is thus no constant pathological change, such as atrophy, in the gastric mucous membrane after death, and in one case of Addison's anæmia, in which a fragment was excised during an operation for appendicitis, Dr. R. D. Passey found no atrophy and no more inflammation than in a specimen obtained under similar circumstances in a case of "benign" achlorhydria.

For the above reasons we believe that Addison's anæmia only develops in individuals who have achlorhydria. The anæmia is caused by hæmolytic toxin absorbed from the intestine, where they have been produced by the action of bacteria coming originally from the mouth, the presence of achlorhydria having deprived the stomach of its antiseptic powers, which normally exert a powerful influence in protecting the bowel from such infection.

II.—DEGENERATION OF THE SPINAL CORD IN ADDISON'S ANÆMIA.

Lichtheim [13] in 1887 described three cases of "pernicious anæmia" with spinal symptoms. A post-mortem performed on two of them showed degeneration of the posterior columns and to a less extent in the lateral columns. His clinical and pathological observations were soon confirmed by Minnich [15] and Nonne [18]; the latter author before long came to the conclusion that his original idea that the degeneration of the spinal cord was secondary to the anæmia must be incorrect and that both conditions were the result of some chronic intoxication.

In the last twenty-five years spinal cord symptoms have been recognized in Addison's anæmia with increasing frequency as they have become more systematically looked for. In 1902 McCrae [14] found them in 25 per cent. of forty cases; in 1918 Woltmann [21] found "indisputable evidence of the destruction of nervous parenchyma" in 80·6 per cent. of 150 cases, which were subjected to a detailed neurological examination at the Mayo Clinic. This corresponds closely with the figures obtained by Minnich [15] [16], who discovered degenerative changes in 77 per cent. of the spinal cords of a consecutive series of fatal cases of "pernicious anæmia."

Mitchell Clarke [17] in 1904 concluded from a study of the literature and from his own cases that the changes in the nervous system in Addison's anæmia could be clearly distinguished from subacute combined degeneration of the cord, whether or not the latter was accompanied by anæmia. We agree, however, with the view expressed by Barker [2] in 1919 that no definite line can be drawn between Addison's anæmia accompanied by changes in the spinal cord, and subacute combined degeneration of the cord accompanied by anæmia. The difference is simply one of degree, and depends upon whether a hæmolysin or a neuro-toxin is the more active. If either toxin is at first produced alone, there is more time for it to give rise to marked changes; thus when Addison's anæmia is severe and rapidly fatal, there may be no time for any nervous symptoms to develop, or, if they do develop, they may be trivial in comparison with those observed in cases in which the nervous degeneration has progressed for many months without any anæmia. There appears to be no essential difference between the clinical symptoms or the pathological changes in the spinal cord except in their severity, whether the nervous degeneration or the anæmia predominates.

III.—NATURE OF THE ANÆMIA ASSOCIATED WITH SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD.

In some of the nine cases described by Risien Russell, Batten and Collier [20] in 1900 no anæmia was present throughout the disease; in others it developed towards the end, whilst in others it was an "obtrusive symptom from the first and preceded the manifestation of nervous symptoms by many months." They definitely state that repeated examinations of the blood "failed to reveal the alterations found in pernicious anæmia," the changes being those characteristic of secondary anæmia. The red corpuscles were generally normal in shape, nucleated cells were only found in one case in very small numbers, and no megaloblasts or microblasts were present.

In 1904, Mitchell Clarke [17] from a study of five cases of spinal cord degeneration in anæmia concluded that it is by "no means only, nor even most often, that the form of anæmia is pernicious anæmia."

In an article on subacute combined degeneration of the spinal cord published in 1910, Collier [10] states that "severe secondary anæmia" is almost invariably present at some period of the disease, though its development is sometimes deferred till the last stages. But though he regarded the anæmia as "definitely secondary," his description of the blood corresponds more closely to that of Addison's anæmia. "The colour index is usually above normal . . . Anisocytosis, poikilocytosis, and polychromatophilia are common. Normoblasts are sometimes numerous." He adds, however, that "megaloblasts have not been found, and the reaction for free iron in the liver has not been obtained in any case," but he makes the important observation that the skin not infrequently assumes a striking lemon-yellow colour.

In the same year Byrom Bramwell [7] described a case in which the nervous symptoms developed three years before the anæmia was obvious, but the blood finally presented all the typical features of Addison's anæmia. Post-mortem excess of iron was present in the liver, and there was a great increase in the red bone marrow; the spinal cord changes were typical of subacute combined degeneration. In 1915 [8] he brought forward further evidence pointing to the anæmia being of the Addisonian variety in subacute combined degeneration of the cord, even when it did not first conform to type. He quotes a case in which rapid changes occurred in the blood during the last fortnight of life, the colour index slowly rising in consecutive investigations from 0·8 to 2·3.

Single cases of subacute combined degeneration of the cord have been described by Taylor and Waterman (1903), Collins (1904), Loudon (1913), and Redwood (1920), and two cases each by Grinker (1908), and Hassin (1917), in which the anæmia was definitely of the Addisonian type. Cadwalader, describing nine cases in 1916, stated his belief that subacute combined degeneration was not associated with any form of anæmia except "pernicious" anæmia.

In his latest article on the subject, published in 1921, Collier [11] came to conclusions entirely different from those in his earlier writings. He states that a careful investigation of the blood changes at various stages of the disease and of the post-mortem findings in a large series of cases, has proved beyond any possible doubt that the blood-changes in every case are identical with those that are met with in the various stages of pernicious anæmia, and that a typical post-mortem picture of pernicious anæmia occurs frequently enough in subacute combined degeneration. In contradiction to his earlier papers he says that "megaloblasts may be found in numbers."

Addison's anæmia, particularly in the early stages and during the periods of remission, may present a blood-picture far removed from what is considered to be typical of the disease. This has been recorded frequently and is the experience of all clinicians. A recent case of undoubted Addison's anæmia, in which numerous blood examinations were made and the diagnosis was confirmed post mortem, illustrates this point clearly (Table I).

TABLE I.—VARIATIONS IN COLOUR-INDEX IN A TYPICAL CASE OF ADDISON'S ANÆMIA.

Date	Red blood corpuscles per c.mm.	Hæmoglobin percentage	Colour index
22.9.21	2,200,000	30	0·7
8.10.21	1,500,000	20	0·6
1.11.21	2,800,000	40	0 7
11.11.21	2,400,000	48	1·2
18.11.21	2,088,000	58	1·4
5.12.21	3,100,000	62	1·0
20.1.22	1,600,000	40	1·25
10.4.22	2,400,000	40	0·8
15.5.22	2,240,000	60	1·3
12.6.22	1,640,000	46	1·4
26.6.22	2,440,000	50	1·0

TABLE II.—BLOOD EXAMINATIONS IN EIGHT CASES OF SUBACUTE COMBINED DEGENERATION OF THE CORD.

Name	Age	Date	Red cells per c.mm.	Hæmoglobin percentage	Colour index	Poikilocytosis	Anisocytosis	Normoblasts	Megaloblasts	Leucocytes per c.mm.	Wassermann reaction
John B. ..	62	12.7.20	2,650,000	66	1·2	+	+	—	—	3,750	Negative
Wm. B. ..	72	—2.22	2,710,000	48	0·88	+	?	—	—	7,000	Negative
		27.6.22	3,200,000	85	1·3	+	+	+	—	5,090	
Thos. M. ..	65	2.3.22	3,500,000	68	0·97	+	+	—	—	9,500	Negative
		27.4.22	4,580,000	68	0·6						
		29.5.22	4,700,000	62	0·65						
		26.7.22	6,150,000	86	0·7						
Edith J. ..	40	30.3.22	3,300,000	58	0·88	—	+	—	—	7,100	Positive (C.S.F. negative)
J. E. W. (male)	52	14.7.19	2,300,000	52	1·1	++	++	+	+		Negative
		29.7.19	1,500,000	54	1·8	++	++	+	+	2,800	
		16.9.19	3,200,000	94	1·5	?	?	+	+		
		3.3.21	3,400,000	70	1·0	+	+	+	—	6,000	
		—3.21	3,140,000	83	1·3	+	+	—	—	3,700	
Margaret H.	64	—2.22	2,860,000	85	1·5	+	+	—	—	?	Negative
Harriet G.	51	—7.22	4,710,000	56	0·6	+	+	—	—	5,800	Negative
Marion H.	42	—7.22	2,380,000	56	1·2	+	+	—	—	7,920	Negative

It would thus appear probable that many of the cases of subacute combined degeneration recorded, including the nine published by Risien

Russell, Batten and Collier in 1900, in which the blood-picture was not characteristic of Addison's anæmia, were none the less associated with Addison's anæmia. The lemon-yellow colour, which Collier observed in many cases before he came to the conclusion that the anæmia was of the "pernicious" type, is quite characteristic of the latter, and, being caused by staining of the subcutaneous fat with pigment derived from hæmoglobin, it affords just as good evidence of hæmolysis as the Prussian-blue reaction obtained in the liver and sometimes in other organs after death. This reaction, although present in almost all cases of typical Addison's anæmia, is sometimes absent in cases of subacute combined degeneration, because the blood destruction has not been sufficiently severe and prolonged.

During the time our present series of eight cases of subacute combined degeneration of the cord was under observation the blood-picture was not typical of Addison's anæmia, but it was quite compatible with an early stage of that condition, and in those cases in which repeated examinations were made the colour index was at times over one, and the film at times showed the characteristic features (Table II).

IV.—Digestive Symptoms preceding and accompanying the Nervous Symptoms of Subacute Combined Degeneration of the Cord.

In 1908 Grinker [12] drew attention to the occasional association of digestive symptoms with subacute combined degeneration of the cord and laid special stress on the frequency of diarrhœa. In 1910 Collier [10] stated that he had occasionally observed symptoms of gastro-enteritis and colitis in the disease. In the same year Farquhar Buzzard [9] stated that gastro-intestinal disturbances may precede or accompany the earliest signs of the nervous disease. In his latest contribution to the subject in 1921, Collier says that in a considerable number of cases symptoms pointing to gastro-intestinal infection, such as vomiting, diarrhœa, anorexia or constipation, were prominent before the onset of nervous symptoms.

In seven of our eight cases digestive symptoms were present. Two patients had had attacks of diarrhœa shortly before the first nervous symptoms appeared; one of these had been actually admitted into hospital on this account. In another case "bilious attacks" with occasional vomiting and attacks of flatulent dyspepsia preceded the nervous symptoms, and in a fourth there was a long history of slight flatulent dyspepsia. In three others the digestive symptoms only appeared after the first signs of nervous disease.

The digestive symptoms, which are so frequently associated with subacute combined degeneration of the cord, are all symptoms which are often caused by achlorhydria apart from this nervous disease and apart from Addison's anæmia, and which are generally controlled without difficulty by the administration of dilute hydrochloric acid. As these symptoms frequently precede the development of the nervous manifestations, just as similar digestive symptoms frequently precede the development of Addison's anæmia, it seems probable that the achlorhydria precedes the development of the nervous symptoms. It is certainly not due to the anæmia, as the degree of this is generally slight, quite apart from the fact that it is exceedingly doubtful whether anæmia ever does give rise to achlorhydria. The fact that digestive symptoms do not always precede the development of nervous symptoms does not make it any the less likely that achlorhydria always precedes them, as the latter condition may be present for years without giving rise to the slightest indigestion, and it is indeed present in about four per cent. of normal young men without digestive symptoms.

V.—Achlorhydria in Subacute Combined Degeneration of the Cord.

We have had the opportunity of investigating eight cases of typical subacute combined degeneration of the cord by the fractional method of gastric analysis. In all of the eight free hydrochloric acid was completely absent throughout the period of digestion. The test was repeated in three of the cases with the same result.

So far as we know no other cases have been investigated in this way. Llewellys Barker [2] found complete achlorhydria in two cases, presumably after an ordinary one-hour test-meal. In one the anæmia at the time of the examination was said to be "quite definitely not pernicious," though the colour index was 1·1, and in the other the red corpuscles numbered 4,000,000 per cm., the hæmoglobin percentage being 90. Barker's observation is valuable confirmation of our results, but the fact that achlorhydria persists throughout digestion is of course of greater significance than the absence of free hydrochloric acid from the contents of the stomach removed in the ordinary way one hour after the meal has been taken. Dr. J. F. Wilkinson, of Melbourne, informs us that he discovered achlorhydria in a patient who consulted him for digestive symptoms a year before the first signs of subacute combined degeneration of the cord appeared.

For purposes of control gastric analyses were made in a series of typical cases of disseminated sclerosis and tabes dorsalis. In eight consecutive cases of disseminated sclerosis achlorhydria was never found, the curves of acidity being the same as would be likely to occur in a series of eight normal people. Of nine consecutive cases of tabes dorsalis one was found to have achlorhydria ; the remainder had curves which fell within normal limits, though in two cases it was somewhat high. As 4 per cent. of normal individuals have achlorhydria, the single case in this series is probably of no importance (Table III).

Table III.—Relative Frequency of Achlorhydria in Various Conditions.

	Number of cases	Achlorhydria		Low acidity	"Normal" acidity	High acidity
		Number	Percentage			
Normal (Bennett and Ryle) [5]	100	4	4	1	87	8
Various medical diseases (Bell) [3]	425	63	14·8	53 (12·5 per cent.)	205 (48·3 per cent.)	104 (24·4 per cent.)
Addison's (pernicious) anæmia	66	64	96	1	1	0
Carcinoma of stomach	10	3	33	3	3	0
Subacute combined degeneration of cord	8	8	100	0	0	0
Tabes dorsalis . .	9	1	11	1	5	2
Disseminated sclerosis	8	0	0	1	7	0

Gastric analysis may therefore give information of real help in diagnosis, the presence of free hydrochloric acid in any fraction of a test-meal being probably a decisive point against the diagnosis of subacute combined degeneration, whereas the discovery of achlorhydria would considerably strengthen the probability of such a diagnosis being correct. In three recent cases, which presented features very suggestive of subacute combined degeneration, a normal curve of gastric acidity was discovered. Each eventually proved to be a case of syphilitic disease of the spinal cord. These cases are analogous with two others, the only cases in Guy's Hospital in which a diagnosis of Addison's anæmia had been made in spite of the fact that free hydrochloric acid was present in the stomach. At the post-mortem no evidence of hæmolysis was present, one being found to have infective endocarditis, and the other, who died of lobar pneumonia, having microscopical changes in the spleen, which were typical of Hodgkin's disease.

VI.—Oral Sepsis.

The importance of oral sepsis in Addison's anæmia has been almost universally acknowledged since Hunter first drew attention to the subject over twenty years ago. In his article on subacute combined degeneration of the cord, published in 1910, Collier states that septic gingivitis and stomatitis are common in the disease. One of our eight patients had had all his teeth taken out on account of severe pyorrhœa shortly before we saw him. Two others had had all removed twenty or more years earlier because they were becoming loose. The remaining five had more or less severe gingivitis with pyorrhœa and septic stumps. Only one patient complained of soreness of the tongue; it was abnormally red and corrugated, but there was no ulceration. In another the tongue was abnormally smooth and shiny, the papillæ having atrophied to a great extent, although the patient, who was edentulous, was unaware that she had ever had glossitis.

VII.—The Evidence of Intestinal Infection in Subacute Combined Degeneration of the Cord and Addison's Anæmia.

Streptococci are almost invariably present in the sockets of septic teeth, whether the individual is otherwise healthy or not, but so far as our observations go the *Streptococcus longus* is not often found in the contents of the duodenum removed during life with an Einhorn tube, except in Addison's anæmia and in subacute combined degeneration of the cord. In four normal individuals and in eight cases of infective jaundice from Gallipoli investigated by one of us (A. F. H.) with C. J. Martin in Lemnos in the autumn of 1915 no streptococci were present. Among fourteen patients suffering from various medical conditions the duodenal contents contained the *S. longus* in only three instances, one being in a patient with diabetes and slight pyorrhœa alveolaris, and the other two men with cholecystitis, one of whom also had a severe infection of his tonsils; in all three cases the gastric secretion was normal. In four of the fourteen cases achlorhydria was present, together with very severe oral sepsis in two and slight pyorrhœa in a third, but in spite of this no streptococci were found. In every one of the seven cases of Addison's anæmia and the four cases of subacute combined degeneration of the cord which we have investigated the *S. longus* was found on microscopic examination and was obtained on cultivation of the duodenal contents. (Table IV.)

TABLE IV.—*Streptococcus longus* IN THE DUODENAL CONTENTS.

	Number of cases	*S. longus* present	Percentage
Normal	4	0	11·5
Infective jaundice	8	0	
Various medical cases	14	3	
Addison's anæmia	7	7	100
Subacute combined degeneration of the cord	4	4	

In spite of the somewhat smaller number of cases, the contrast between the 11·5 per cent. of controls, in which streptococci were found, with 100 per cent. of subacute combined degeneration of the cord and Addison's anæmia, is so striking that the conclusion can probably be drawn that an infection of the intestine with a *S. longus* is an essential factor in the production of these diseases. In any case the presence of the *S. longus* in the duodenum is evidence of active infection of the intestine. In one of our patients an autogenous vaccine made from the *S. longus* isolated from the socket of an infected tooth gave rise to a temporary aggravation of the sensation of pins and needles in the hands and feet each time it was injected.

VIII.—DISEASES OTHER THAN ADDISON'S ANÆMIA WHICH MAY BE ASSOCIATED WITH SUBACUTE COMBINED DEGENERATION.

Schultze, Nonne and Geitlin are said to have reported cases of subacute combined degeneration of the cord, in which the blood picture was that of lymphatic leukæmia, and Collier refers to a similar case observed by Greenfield. I only know of two cases of lymphatic leukæmia in which a fractional test meal has been carried out. In one of these complete achlorhydria was present, but in the other the curve was normal. It is obvious that no conclusions can be drawn from the two cases, but the presence of achlorhydria in one of them would suggest that in leukæmia the oral sepsis and achlorhydria, which are the necessary conditions for the development of Addison's anæmia and subacute combined degeneration of the cord, may be present. This would explain the occurrence of cases of so-called "leukanæmia," in which the blood picture is a combination of leukæmia and Addison's anæmia, as well as those rare cases of subacute combined degeneration of the cord with leukæmia which have just been mentioned.

It is also said that severe cachexia may be associated with similar changes in the spinal cord, but we have been able to find no detailed description of such cases, the majority of which appear to have been due to cancer of the stomach. In 30 per cent. of our cases of gastric cancer complete achloryhdria was found with the fractional test meal, and oral sepsis is of course not uncommon. Severe anæmia is more common in cancer of the stomach than in cancer elsewhere. This may be due to the fact that a hæmolytic toxin is sometimes produced when achlorhydria is present and causes a more severe anæmia than would result from the cancer toxins alone. At the same time neuro-toxins might well be produced.

Lastly, subacute combined degeneration of the cord is said to occur in connection with Addison's disease, although here again we have been unable to find any detailed reports. We have, however, had under observation a man suffering from typical Addison's disease with an extreme degree of pigmentation, a very low blood pressure, general asthenia and vomiting, in whom signs of posterior and lateral cord degeneration were present. Further investigation showed that the Addison's disease was associated with the blood changes of Addison's (pernicious) anæmia, so that the nervous changes can be regarded as a complication of the latter rather than of the suprarenal disease.

IX.—Subacute Combined Degeneration of the Cord without Anæmia.

It has generally been stated that cases of subacute combined degeneration of the cord occur without any anæmia. We have, however, seen no reports of such cases, in which blood examinations have been made during the last two or three weeks of life, and Byrom Bramwell's case, in which anæmia of a typical Addisonian form developed during the fortnight before death, shows how necessary it is to do this before concluding that the nervous disease runs its whole course without being complicated by anæmia. It would, however, not be surprising if in a small proportion of cases no anæmia occurred at all, because there is no reason why in some cases neuro-toxins might not be produced without hæmolysins, just as the latter are certainly produced in a considerable number of cases without the former.

X.—Pathogenesis.

In their classical account of subacute combined degeneration of the spinal cord published in 1900, Risien Russell, Batten and Collier [20] came to the conclusion that the disease is caused by some toxic agent, which is also the cause of the anæmia, with which it is generally associated, and that it is not secondary to the anæmia. Writing ten years later, Buzzard [9] suggested that this toxin has its origin in the alimentary canal, and in 1921 Collier [11] concluded that the toxic agent responsible both for the nervous degeneration and the anæmia is of gastro-intestinal origin.

We have already given our reasons for believing that achlorhydria is an essential predisposing cause of Addison's anæmia. Our observations lead us to agree with Collier's most recent conclusion that the anæmia with which subacute combined degeneration of the cord is almost always associated is the so-called " pernicious " form, first described by Addison. It is therefore not surprising that achlorhydria appears to be present as constantly in cases in which subacute combined degeneration of the cord is the earlier and more prominent symptom, as in those in which anæmia is present alone or in which the nervous symptoms remain comparatively unimportant.

Gastric juice has two functions : it helps in the digestion of proteins, and the antiseptic action of its acid helps to protect the intestines from infection with swallowed organisms. In achlorhydria proteins pass into the duodenum in an unaltered form, and bacteria from the mouth and nasopharynx are likely to reach the intestine in far greater numbers than under normal conditions. If achlorhydria is associated with oral sepsis, secondary infection of the intestines is extremely likely to occur. The investigations of Bennett and Dodds [6] show that pancreatic secretion is also deficient in Addison's anæmia. The digestion of proteins is therefore likely to be even more deficient than in cases in which achlorhydria is present alone. Consequently in Addison's anæmia and in subacute combined degeneration of the cord intestinal infection is likely to be associated with the presence in the intestines of excess of undigested or incompletely digested protein. Under such conditions it is not surprising that toxins are produced by the bacterial destruction of proteins in abnormal quantities in the intestines. It is probable that one of these is specially toxic for the blood and leads to a hæmolytic form of anæmia, and that another is specially toxic for nervous tissues and leads to combined degeneration of the spinal cord. In most cases the former toxin is the dominant one, but in a small minority of cases the latter is the more important. Although one or other may appear to be present alone in the early stages, it is rare for the hæmolytic toxin and still more rare for the neurotoxin to continue to be produced without the other throughout the course of the illness.

XI.—TREATMENT.

The most important part of the treatment of subacute combined degeneration is to attempt to overcome the intestinal infection and so stop the development of the neurotoxic and hæmolytic poisons. Oral sepsis should be thoroughly dealt with. Every tooth which shows the slightest sign of infection on expert clinical examination should be condemned. An X-ray photograph should always be taken of all the remaining teeth, however healthy they may appear, and the slightest sign of apical infection or periodontitis should lead to their removal. In most cases every tooth will have to be extracted. If the tonsils are infected they should be enucleated, and the nose and nasal sinuses should also be examined and if necessary thoroughly treated.

The achlorhydria should be corrected by the administration of large doses of hydrochloric acid. In most cases we have found that a drachm and a half of dilute hydrochloric acid are required in order to compensate for the deficiency of gastric juice (Charts I and II). The acid should be added in the proportion of a drachm to 4 oz. of water in order to make a beverage, the acidity of which is about the same as that of gastric juice. If lemon juice and sugar are added the drink is quite palatable. It should be drunk during the course of each meal, and a little of it should be left over to sip for half an hour after the meal is completed. The patient should continue to take it without intermission for the rest of his life, as even if the intestinal infection appears to be overcome, the achlorhydria probably always remains.

Milk which has been soured with an active lactic acid bacillus should also be given for an indefinite period. Most patients can take half a pint three times a day without difficulty.

Lastly, a vaccine should be made from any streptococcus which can be isolated from the sockets of extracted teeth, from the duodenal contents withdrawn through an Einhorn tube, from the fæces and from the urine. This should be given in carefully graduated doses, beginning with very little, and slowly increasing, but it is desirable that no general reaction should follow the injections.

Unfortunately the degeneration of the spinal cord, when it has once occurred, is permanent, so that all that can be expected from adequate treatment of the intestinal infection is that the progress of the disease may be arrested. A certain amount of improvement may, however, result from a systematic course of exercises of the type that Frenkel introduced for tabetic ataxy. On the other hand, if the production of hæmolytic toxins is arrested, the blood shows spontaneous improvement, and recovery can also be accelerated in severe cases by one or more transfusions of blood. Arsenic may be given, but care is necessary, as in the presence of subacute combined degeneration it is difficult to recognize the earliest symptoms of arsenical neuritis.

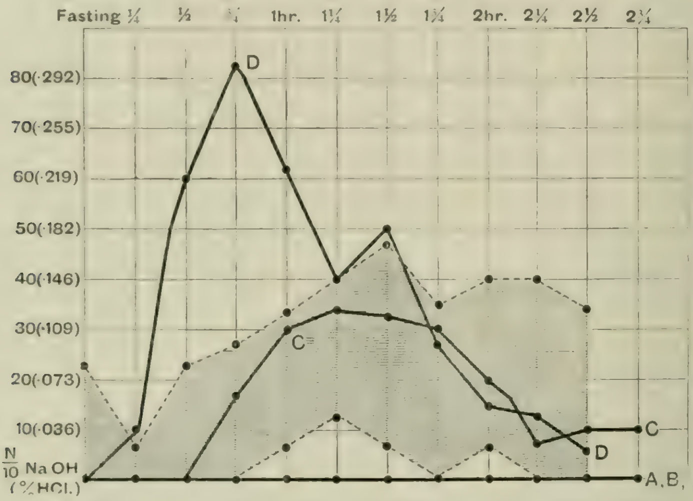

CHART I.—Fractional test meals to show free HCl in a man with subacute combined degeneration of the spinal cord. A, without addition of acid—complete achlorhydria; B, with addition of ʒi dilute HCl (B.P.) in ℥iv water (= 0·3 % HCl) taken with the gruel and also sipped for an hour afterwards; C, with addition of ʒiss dilute HCl in ℥vi of water—normal curve; D, with addition of ʒii dilute HCl in ℥viii water—hyperchlorhydria curve. The shaded area represents the limits for free HCl of 80 % of normal people.

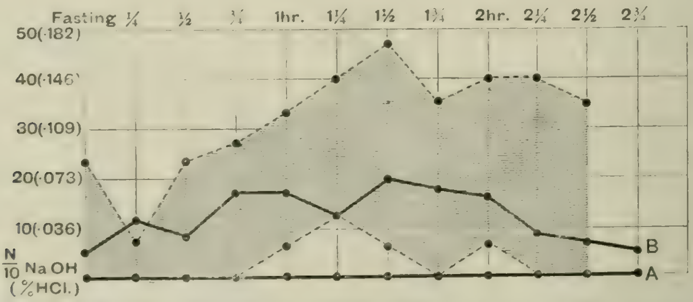

CHART II.—Fractional test-meals to show free HCl in a woman with subacute combined degeneration of the spinal cord. A, without addition of HCl—complete achlorhydria; B, with addition of ʒiss dilute HCl in ℥vi water.

Insufficient time has elapsed to be able to report the final result of treatment on these lines. So far it has been most promising. The anæmia, being recognized at an early stage, rapidly improves; in the two cases of our series which have been longest under observation it has actually disappeared, and in one of these the red corpuscles now number over 5,000,000 per cubic millimetre. There has been no increase in the nervous symptoms or physical signs, and in one of the two cases just referred to the tingling of the feet and hands has almost disappeared, and the ataxic and spastic gait has greatly improved, but the physical signs are unaltered.

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[9] BUZZARD. *Clin. Journ.*, 1910, **36**, 374.
[10] COLLIER. Allbutt and Rolleston's "System of Medicine," London, 1910, **7**, 786.
[11] *Idem.* "Oxford Medicine," 1921, **6**, 356.
[12] GRINKER. *Journ. Amer. Med. Assoc.*, 1908, **50**, 1109.
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[14] MCCRAE. *Journ. Amer. Med. Assoc.*, 1902, **38**, 148.
[15] MINNICH. *Zeitschr. f. klin. Med.*, 1892, **21**, 25 and 264.
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[18] NONNE. *Deutsch. Zeitschr. f. Nervenh.*, 1895, **6**, 313.
[19] *Idem.* *Ibid.*, 1899, **14**, 192.
[20] RUSSELL, BATTEN and COLLIER. *Brain*, 1900, **23**, 39.
[21] WOLTMANN. Collected Papers of Mayo Clinic, 1918, **10**, 933.

THE MENINGIOMAS (DURAL ENDOTHELIOMAS): THEIR SOURCE, AND FAVOURED SEATS OF ORIGIN.[1]

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THE tumours under consideration have long masqueraded under so many guises that it is well-nigh impossible, historically, to do them justice. In their gross appearance, they are sufficiently striking to have attracted the notice of morbid anatomists from early times, and without carrying the subject farther back than Cruveilhier we may feel assured from the admirable illustrations in his famous "Anatomie Pathologique," that he at least had encountered before 1835 some four or five examples in the course of his extensive post-mortem studies.

As these, or similar tumours, were then known occasionally to involve and absorb the adjacent bone, a lively discussion had arisen as to whether they took their origin from the diploe or dura, and if from the dura whether from its internal or external surface. Earlier writers had referred to the lesion as a *fungus duræ matris*, a term which has survived to our times; but Cruveilhier substituted for this the designation *tumeurs cancéreuses des méninges*, thereby reflecting the pathology of his day, and as late as 1858 we find R. Bennett in this country using the term *epithelial cancer* for these meningeal tumours. Such epithets as these, however, could not survive the advent of the morbid anatomist armed with the microscope and aniline dyes, nor in turn the embryologist with his classification of tissues.

In the early days of histological pathology which had such an impetus in the 'fifties and which Sir James Paget in this country, the pupils of Johannes Müller in Germany, and Hermann Lebert, a disciple of Dupuytren, in Paris, had done so much to advance, it was customary to give descriptive designations to tumours. In 1854, in his celebrated lectures on surgical pathology, Paget confessed his inability satisfactorily to classify the large group of tumours "less malignant than cancer," to which Lebert had given the name *tumeurs fibro-plastiques.*

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[1] The Cavendish Lecture, delivered before the West London Medico-Chirurgical Society, June 13, 1922.

He suggested the term *myeloid* or "marrow-like."[1] Billroth in 1856 gave the name *cylindroma* to a growth of the orbit which showed a peculiar tubular form of hyaline deposition, and at about the same time another term, still in common use for certain growths in which so-called "brain-sand" abounds, was first employed by Virchow. He had been among the first to call attention to the calcareous granules which, unrelated to any tumour growth, are found deposited in various situations in the cerebral appendages and meningeal envelopes. Though uncertain of their nature and origin, on finding these "sand-bodies" prevalent in two small dural tumours which had come to his attention, one arising from the olfactory groove and the other from the porus acusticus, he named them *psammoma*.[2]

Thus, names which are merely descriptive of degenerative processes of common occurrence in the tumours in question have since come to be widely employed.

At about this time there was a tendency among French writers, notably by Bouchard (1864), and by Robin [21], to substitute *epithelioma* for Lebert's "tumeur fibro-plastique," and when one considers that Robin was employing the current terminology for the lining of the serous spaces and vessels, and that he regarded the cells of the arachnoid as the source of origin of the growths, he deserves due credit for his views. This, however, was brushed aside by the greater authority of Rudolph Virchow.

In his classical "Vorlesungen" [23], though making some exceptions in regard to the psammomas, Virchow incorporated the tumours in question under the term *Sarkome der Dura mater*, and they continue for the most part to be so classified. However, in spite of their tendency to invade or absorb the bone, it came to be recognized that they were benign lesions of a peculiar histogenesis for which the designation sarcoma was inappropriate and misleading, and by the 'seventies this, in its turn, had begun to be qualified. Accordingly, such terms as

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[1] In his celebrated "Anatomie Pathologique Générale," Paris, 1857 and 1861, Lebert describes and pictures as fibro-plastic tumours of the dura a few examples of these lesions, and in his "Surgical Pathology," Paget cites a most extraordinary example of a myeloid tumour which must have been a widespread bilateral and parasagittal meningioma with extensive hyperostosis cranei. The preparation is still in the Museum of St. Bartholomew's Hospital.

[2] Virchow came to regret the introduction (1859) of this term, because of its misuse by others. In a later article [24] he expressly states that an epithelial or endothelial tumour containing concrements is not a psammoma, that true psammomas have a connective tissue groundwork. This statement merely added to the existing confusion, though it is fair to say that psammoma bodies are apt to be more numerous in the older and more fibrous forms of meningeal tumours.

alveolar sarcoma came into use, and in France Cornil with Ranvier substituted *sarcome angiolitique* for Virchow's psammoma. But the term, sarcoma, however qualified, could not permanently survive the changing terminology of the embryologists.

Camillo Golgi, in an important article published in 1869 [14], called attention to the existing confusion in regard to these tumours. He had an opportunity to study two specimens, one of which was a typical tumour of the ethmoid region, which had come to light at autopsy in the hospital at Pavia, and he was the first to suggest the term *endothelioma* out of consideration for the employment by His of the word endothelium as opposed to epithelium. Thus, the simple term endothelioma was introduced in Italy, whence it has gradually made its way into other countries, but, unfortunately, even in the country of its birth, cumbersome word-combinations soon became attached to it. Bizzozero and Bozzolo [4], for example, soon subdivided the dural endotheliomas into three types, as *sarcoma endothelioides alveolare*, *sarcoma endothelioides fasciculatum*, and *fibroma endothelioides*, according to the manner in which the connective tissue elements behave in their relation to the endothelial cell nests, and whether endothelial or fibroblastic elements predominate. In this fashion, during the fifty years which have since passed, pathologists have vied with one another in modifying and extending the qualification "endothelial" to a wide range of tumours in a great variety of situations, in bone, thyroid, parotid, ovary, and elsewhere, into peritheliomas, hæmangio- and lymphangio-endotheliomas, and so on, with such hair-splitting refinements as to produce histological chaos.

In consequence of all this, the striking and characteristic intracranial growths we are considering, to which many of these names were first attached, have become so obscured by a multiplicity of designations that it is highly desirable to rescue and to re-assemble them under some simple caption. For this, Golgi's term, which has in later days gradually come to prevail, might suffice; but even this is now of questionable advantage, for it seems quite probable that, though attached to the dura, the tumours do not arise from this membrane proper, but rather from elements of the arachnoid which project into it; nor are they, in the parlance of some embryologists, tumours which, strictly speaking, actually originate from what are to be considered endothelial elements.

Not everyone has adopted Minot's "mesothelium" even for the cells lining the serous cavities, and it is quite evident that he had no intention of including the meningeal spaces in this category, as some appear to have taken for granted. However, should the term be thus extended, and many anatomists so employ it, *arachnoideal mesotheliomas* would be the proper name for these tumours. But even if correct, this designation is too cumbersome for convenience, and it would seem best to sweep all these terms aside and adopt a label which is simple, and at the same time non-committal, except in so far as it indicates that the growths in question arise from the meninges. For this purpose the term *meningothelioma* was first proposed, but it has, on further consideration,[1] been shortened to *meningioma.* This word, consequently, will be used to indicate the entire group of tumours which appear to arise from the pachymeninx, whether mesothelial or fibrous elements predominate; whether the overlying bone shows hyperostosis or is unchanged; whether the growth is pedunculated or flat and widespread, and regardless of the degenerative changes and the presence or otherwise of psammoma granules.

These tumours, the meningiomas, have, as we shall see, favourite seats of origin and, though they may differ considerably in their histological picture, they are, as a rule, easily recognizable not only by their gross appearance but because of the fact that the stalk from which in their simpler form they seem to arise is so intimately incorporated with the dura that they appear to originate from it.[2]

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[1] A note regarding the derivation of "thelium" and its combinations may not be amiss, and for the basis of what follows I am indebted to my colleague Frederick T. Lewis. The term *epithelis* (from ἐπί = upon; θήλη = the nipple) appears to have been introduced by Ruysch early in the eighteenth century, and was first used for that transitional part of the epiderm at the lips and nipple—though in time "epithelium" came to be generally used not only for the two peripheral germ layers but for the lining of the serous and vascular spaces as well. In 1865 the word *endothelium* was first used by His as a designation for the lining membrane of these cavities arising from mesenchymal cells within the middle germ layer, and the term has come into general use not only for blood-vessels and lymphatics but all serous cavities as well. Kölliker in 1882 had used the term *mesepithelium* for the lining of the body cavities and urogenital epithelium, reserving the term endothelium for the vessels, synovial cavities, meninges, and so on; and to the same tissues Minot a few years later gave the name *mesothelium.* All three terms, *epi-*, *endo-*, and *mesothelium*, would appear to be unfortunate in view of their derivation in part from θήλη, but they, nevertheless, have come to convey an idea.

[2] There are a few tumours which possibly are allied to the meningiomas, but which have no dural connection: they appear to arise from the pia. They are rare tumours of an angiomatous nature, whereas those under discussion are relatively non-vascular. Another still more rare tumour (particularly so in man) is the so-called cholesteatoma of the choroid plexus. It is actually an endothelioma with extensive psammoma deposit, and is often bilateral.

INCIDENCE.

Some years ago all of the material relating to the several meningiomas, intraspinal as well as intracranial, then included in my tumour series, was gathered with the intent of publishing in detail our clinical and operative experiences with these interesting lesions. This project, however, was interrupted by the discovery that the acoustic tumours (neurinomas of Verocay), which in several instances had been diagnosed as fibro-endotheliomas, were distinctive tumours of an entirely different order. The " endotheliomas " were consequently dropped for the time being, in order to make a more thorough study of the tumours originating from the eighth cranial nerve, commonly described, in view of their location, as tumours of the cerebello-pontile angle.

In a monograph ultimately published on the subject of the acoustic tumours [8] it was pointed out that these lesions when bilateral are not infrequently accompanied by multiple small meningeal endotheliomas, so that tumours of these two types (neurinoma and meningioma) are in certain respects related. Nevertheless, it is far more usual for one or the other to occur in isolated form, and until something more is learned of a common ætiological factor it is undoubtedly best to consider them apart and as distinctive lesions.

The time has long since passed when we could hope to advance our knowledge of intracranial tumours to any great extent by considering them as a whole. Even their mechanical or pressure effects, which might be expected to be more or less similar in all cases because of the rigid character of the bony chamber within which they arise, differ widely, and it is notably true of these meningiomas that they may attain a huge size without giving rise to any of the so-called cardinal symptoms of tumour, notably headaches and objective changes in the eye-grounds.

Intracranial tumours, indeed, are so protean in form ; they behave in such different ways ; they provoke such varied clinical pictures ; and the proper method of dealing with many of them, even when they are exposed by an operation, is in many cases still so problematical, that our only hope for progress is to particularize on certain groups of cases.

There are three ways in which a large material such as is before us may be profitably attacked. We may (1) concentrate our attention upon tumours of certain histogenetic types whatever their situation ; (2) we may study tumours of all types in a given situation ; or (3) what is perhaps better still, we may restrict our analysis, as was done with the acoustic tumours, to tumours of a single type in a given situation.

Only by the adoption of one of these methods can one's casual acquaintance with a disorder, made at the bedside or operating table, ripen into familiarity. Each has its advantages, but for the purposes of this particular study I shall adopt the first, and consider the meningiomas as a whole.

VERIFIED MENINGIOMAS.

On various occasions an explanation has been given of the system under which the tumour cases of my clinic are classified. They are listed as (1) *tumour verified*, when the character of the lesion has been histologically determined at operation or autopsy ; as (2) *tumour unverified*, when the presence of a growth is reasonably certain or, indeed, when it may actually have been seen but without removal of a fragment for verification ; and as (3) *tumour suspect* to include those cases referred to the clinic with a presumptive diagnosis of tumour, of the justification of which there remains considerable doubt.

In our present connection we are interested only in the 751 verified intracranial tumours, and without going into the detail, unnecessary for our present purposes, of distinguishing between the various sub-varieties of gliomas, adenomas, and so on, the cases may be tabulated as follows, in order to indicate the ratio of the meningiomas to other main tumour groups.

TABLE OF VERIFIED INTRACRANIAL TUMOURS TO MARCH 15, 1922.

Gliomas		314 cases	(41·8 per cent.)
Adenomas (chiefly pituitary)		159 ,,	(21·2 ,,)
Meningiomas		85 ,,	(11·3 ,,)
Neurinomas (acoustic)		63 ,,	(8·4 ,,)
Congenital tumours		40 ,,	(5·3 ,,)
(*a*) Suprasellar tumours (chiefly of pharyngeal pouch origin)	28		
(*b*) Cholesteatomas, dermoids, and teratomas	12		
Granulomas		33 cases	(4·4 per cent.)
(*a*) Gummas	12		
(*b*) Tubercles	21		
Papillomas (choroid plexus)		11 cases	(1·5 per cent.)
Angiomas		7 ,,	(0·9 ,,)
Metastatic and invasive		27 ,,	(3·6 ,,)
Miscellaneous and unclassified		12 ,,	(1·6 ,,)
		751	

The meningiomas, as can be seen, stand in about a one-to-four ratio to the gliomas or brain tumours proper, and if we add to this intracranial group of eighty-five cases twelve others which have arisen in the spinal canal, there are, at the time of writing, nearly 100 tumours to deal with.

Anything like a complete analysis of these cases would far exceed the possibilities of a single address if the innumerable questions which would naturally arise were answered with any measure of completeness. The interest of the physician and neurologist would centre on the symptomatology and diagnosis--particularly upon the mistakes in diagnosis, and in these the psychiatrist, for reasons to be pointed out, is concerned perhaps more than any other. In the province of the ophthalmologist lie the visual field distortions, the examples of unilateral exophthalmos, and, above all, the changes—or what is possibly more important, the lack of changes—in the eye-grounds, for a choked disc may be absent or at least long delayed; on the other hand, in the suprasellar lesions a primary optic atrophy may be the essential guide to the site of the lesion. Some of the tumours originate near the porus acusticus with loss of hearing as an early symptom, and so concern the otologist. Others which arise from the olfactory groove and invade the ethmoid cells come into the province of the rhinologist, and that newest of specialists, the endocrinologist, doubtless may have difficulty in distinguishing primary pituitary disease from the dyspituitarism secondary to one of these growths which so commonly arise from the meninges bridging the sella. And, last of all, the interests of the surgeon are focused on the methods employed for the removal, particularly of the more inacessible of these tumours, and upon the end results which may be obtained. Being one of them myself, the temptation is strong to yield to the desires of my own kind, and yet, in view of the very seriousness of his therapeutic measures, it behoves the surgeon, even more than others, to know all that he can learn regarding the origin, site, and characteristics of the lesion he plans to attack before he goes into action. I propose, therefore, though it is a somewhat less exciting story, to confine myself on this occasion largely to the two points mentioned in my title—the source, and the seats of predilection of the meningiomas.

The Source of the Tumours.

In 1911 an opportunity was afforded for an enlightening post-mortem study of one of these growths which had been undisturbed by previous operative manipulations. Including three spinal tumours, it was the fifteenth case in the series, and we were then still labouring under the impression that the growths took origin from the dura and were of various kinds. Most of the preceding tumours had possessed a broad base of meningeal attachment, and until this case no particular attention had been paid to the meninges remote from the lesion, except to note the presence of multiple herniations which had early aroused our interest.

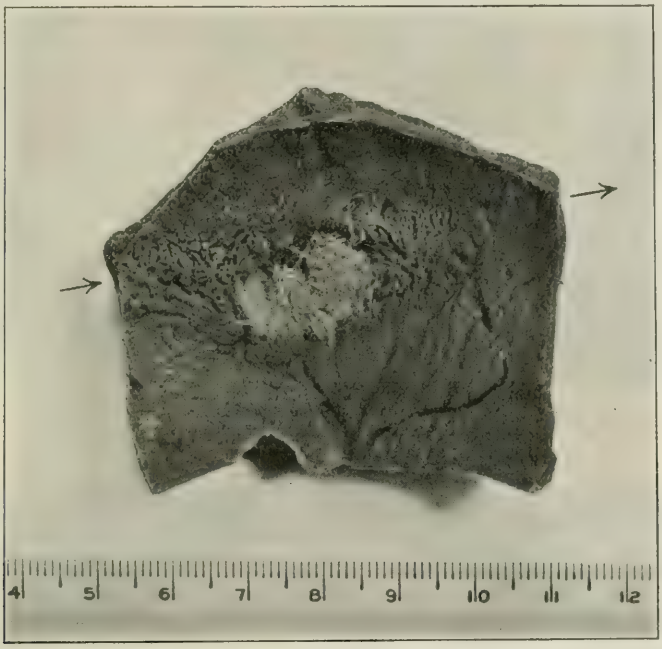

FIG. 1.—Fragment of calvarium overlying point of origin of tumour, showing slight invasion of inner table without hyperostosis. (Arrows show groove of sinus sagittalis.)

The patient, a woman aged 41, was admitted to the John Hopkins Hospital in a profound stupor, obviously in the terminal stage of compression from a brain tumour. An incomplete story was secured from a relative, of headaches for many years, of five months' confinement in bed with increasing disability of her left side, of progressive mental impairment, and finally of somnolence. She succumbed twenty-four hours after a first-stage osteoplastic procedure, at which time the dura was not opened. Had her condition at this first session justified a more prolonged exploration with exposure of the brain, the tumour would in all probability not have been disclosed, in view of its small surface area confined to the mesial edge of the hemisphere.

As is our custom at autopsy when circumstances permit, the brain was fixed before removal by a formalin perfusion through the carotids in order to preserve the pre-existing distortions which are otherwise considerably modified. On removal of the calvarium there was disclosed, about 5 cm. anterior to the Rolandic point, a small area (fig. 1) overlapping the groove of the

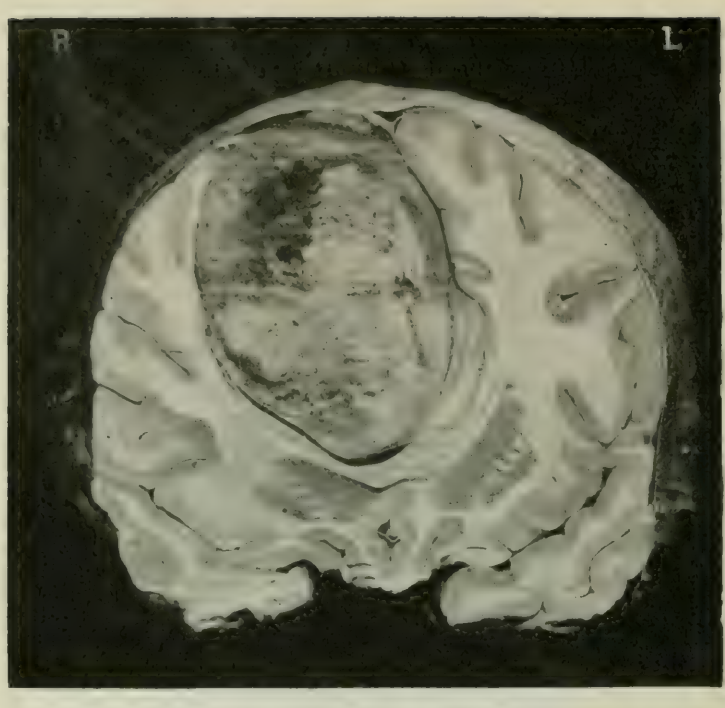

FIG. 2.—Coronal section through tumour, viewed from before, showing great dislocation of falx and corpus callosum.

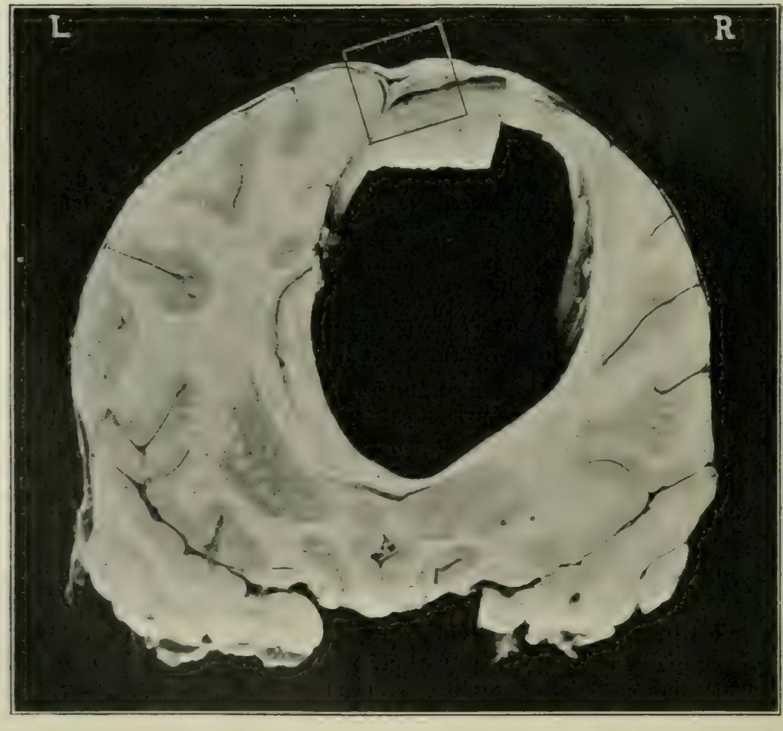

FIG. 3.—Coronal section viewed from behind, showing cavity occupied by the tumour and its only point of attachment under the lateral expansion of the sinus and at the angle of the falx.

sagittal sinus where the dura was adherent. The brain was removed, so far as possible, with its dural envelope intact, and a coronal section, through the point where the adhesions had been noted, transected a large tumour (fig. 2). of about 150 grm. weight, which had greatly deformed the hemisphere, and practically obliterated the ventricles. Except for the small stalk, from which the growth evidently arose, situated in the parasagittal angle and underlying the parasinoidal expansion of the sinus, the tumour was nowhere adherent (fig. 3). Hence, though apparently within, it actually lay outside of the hemisphere, whose pial covering remained intact over the deformed convolutions.

Microscopic sections through the point of meningeal attachment showed (fig. 4) that the tumour had invaded the sinus without thrombosing it, and though traces of the intervening dura still remained, it had been so effectually destroyed that to regard the sinus wall as the starting-point of the growth was an inevitable conclusion.

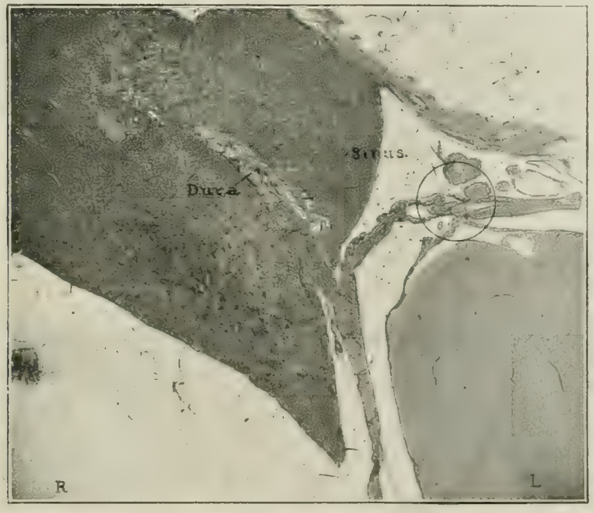

Fig. 4.—Section from area of attachment (squared area of fig. 3), showing invasion of sinus by tumour on right, and on left the arachnoid villi and cell clusters.

The lesion itself presented in different areas a most varied appearance. In some areas (fig. 5) it had a fibromyxomatous appearance, but for the most part (fig. 6) there were masses of endothelial cells with a more or less well-marked alveolar arrangement surrounded by bands of fibrous tissue, the cells of which in some places formed large fibrous whorls. Many areas showed extensive hyaline degeneration, and psammoma bodies together with so-called corpora amylacea were in abundance.

There is nothing unusual in the foregoing description of this particular tumour, for which a variety of names might be used. It

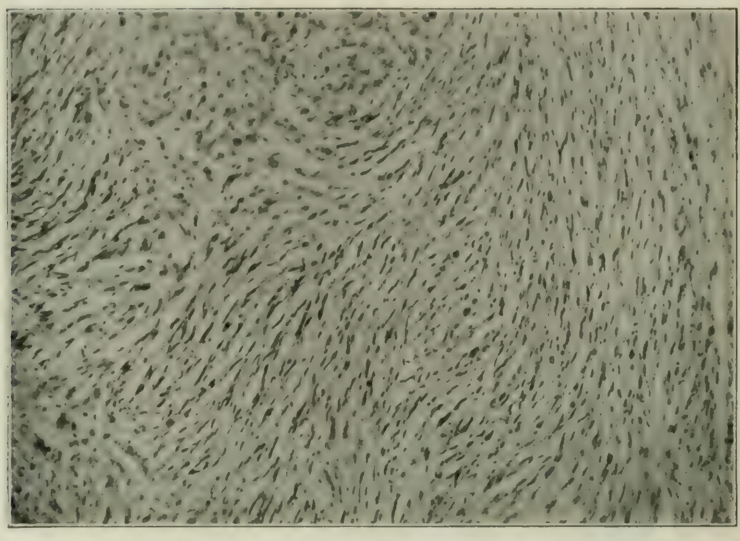

FIG. 5.—Fibromyxomatous area (mag. × 100).

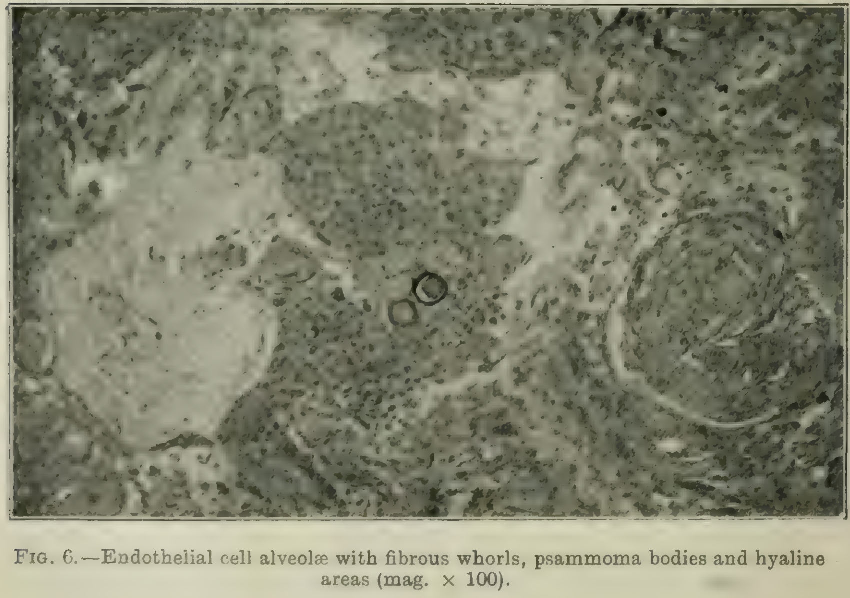

FIG. 6.—Endothelial cell alveolæ with fibrous whorls, psammoma bodies and hyaline areas (mag. × 100).

would probably deserve the term fibro-myxo-endothelio-sarcoma, and its seeming invasion of dura and bone would justify the assumption that it had malignant qualities which in time might have produced metastases. The whole story is essentially commonplace, and tumours of corresponding nature, beyond enumeration, have from time to time been reported in the literature.

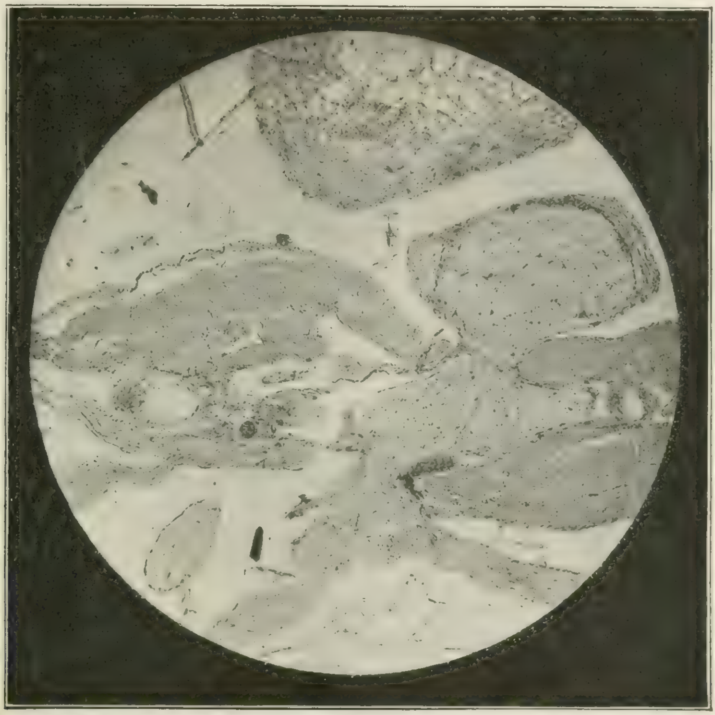

FIG. 7.—Showing an arachnoid villus projecting through dura into sinus. Also nests of arachnoid cells and psammona body lying within dura. (Area circled in fig. 4.)

But something apart from all this, of importance in our present connection, was observed in the meninges remote from the tumour. As already mentioned, the brain after fixation[1] had been removed with its meninges largely intact, and sections through the unusually small stalk of the tumour gave a definite clue to the histogenesis of the lesion. Projecting into the sinus on the side of the uninvolved hemisphere were a number of hypertrophied arachnoid villi (fig. 7), capped by clusters of endothelial cells of precisely the same character and staining reactions as those of the alveolated masses of cells comprising the bulk of the tumour. Many of these cell-clusters disclosed in the dura showed a tendency to the familiar whorl formation (fig. 8), and in association with them were psammoma bodies in considerable numbers, In short, scattered through the uninvolved and presumably normal meninges were all the elements characterizing the tumour proper, these elements being of arachnoidal rather than of dural origin, though encased within the latter membrane.

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[1] A word in regard to this may not be amiss, for I believe that nothing has served to further our understanding of the mechanical effects of tumours so much as the abandonment of the time-honoured method of handling and sectioning the unhardened brain at autopsy after removing the calvarium and stripping off the dura. This unfortunate procedure, which is still an habitual one, has done much to delay our knowledge, particularly of the secondary disorders in cases of brain tumour which concern the cerebrospinal fluid pathway in ventricles, cisternæ and leptomeninges. For not only is the tumour topography largely altered if fluid escapes before the tissue has been fixed, but with the meninges stripped from the brain there has been little incentive in the past to study them in their relation to the adjacent cortex.

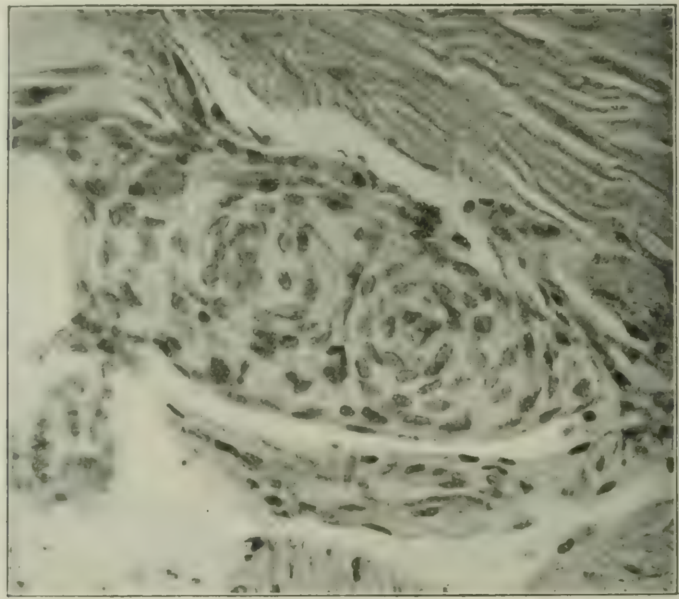

FIG. 8.—Showing typical cluster of arachnoid cells arranged in whorls and lying within dural layers remote from tumour.

This observation, so enlightening to us eleven years ago, proved, as will be seen, to be by no means an original one. It gave us, nevertheless, a new conception of the possible source of origin of these interesting tumours and suggested studies in two directions, the first of which might not have been so vigorously pursued had we then been aware that our views were far from being novel. We undertook, on the one hand, a detailed study of the meninges in areas distant from the tumour in all similar meningeal growths; on the other hand, we began to investigate the arachnoid villi, and this in due course led us into a consideration of the cerebrospinal fluid circulation as a whole.

During the first two years after my transfer in 1912 to Boston, these studies, which had been started in the Hunterian Laboratory at the Johns Hopkins some time before, were continued in collaboration with Lewis H. Weed in the Laboratory of Surgical Research at Harvard, and due largely to his unusual gifts as an investigator considerable progress was made. In the series of papers which were published in 1914 [10], special attention was paid to the arachnoid villi whose function as points of escape for the fluid from the arachnoid spaces into the dural sinuses, though previously surmised, Weed, for the first time I believe, conclusively demonstrated.[1] The villi, in short, appeared to us to play a far more important physiological rôle than had been commonly ascribed to them. But before considering further this aspect of the subject and its bearings upon the tumour question, it is proper to make due acknowledgment to at least three authors by whom our views regarding the origin of these tumours proved to have been anticipated. It is not at all unlikely that there may have been others who have expressed similar ideas in papers under obscure titles which have not come to my attention.

In a brief article published in 1864, John Cleland [7], late Professor of Anatomy in Glasgow, set forth with prescience, the more remarkable when one considers the source of his material for study, the view that two tumours which he had found in the dissecting room, one of them arising from the cribriform plate and the other from the right frontal region adjacent to the superior longitudinal sinus, took their origin from the arachnoid rather than the dura. He observed that in structure they resembled the Pacchionian granulations in a number of points; that connective tissue bands ran through them, that concretions were present in both tumours, and new bone formation in one of them. In pointing out the proximity of these tumours to the falx, he mentioned the bony plaques often found attached to this membrane, and in agreement with Rokitansky attributed them also to the arachnoid rather than to the dura. Similarly, Ch. Robin [21] in France, described in 1869 two tumours likewise met with in the dissecting room. He also attributed them to the arachnoid, and in a long and scholarly article made a strong plea for their epithelial origin.

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[1] On his return to Baltimore, Weed's further pursuit of these investigations led, among other papers, to the publication of his monograph ("The Development of the Cerebrospinal Spaces in Pig and Man." Contributions to Embryology, No. 14. Carnegie Institution of Washington, Publication 225, 1917) on the development of the arachnoid, which represents the most important advance in our knowledge of the meninges since the classical work of Key and Retzius.

In another more extensive study published ten years before our interest in the matter was first awakened, Martin B. Schmidt, of Zürich [22], likewise called attention to the probable relation of the Pacchionian granulations to the so-called sarcomas and psammomas of the dura. In the course of his post-mortem examinations Schmidt had chanced to encounter twelve small meningeal tumours which he made the subject of special study. He was led to make a thorough histological survey of the meninges, and gave the first clear description of the microscopic islands of endothelial cells (Zellzapfen) which are found between the layers of the dura, in numbers which increase with advancing age in practically all individuals.[1] He recognized that these cell masses are related to the arachnoid tufts or villi, that they are themselves unquestionably of arachnoid origin, that they have certain seats of predilection, and, inasmuch as the cells comprising them were identical with those in the small tumours he had studied, he came to the same conclusion that Cleland and Robin, on less sufficient evidence, had reached years before, that they were the starting-point of these growths which, therefore, strictly speaking, have a leptomeningeal rather than pachymeningeal origin.

In medicine perhaps more than in other walks, discoveries are constantly being re-made and views being readvanced, for knowledge spreads slowly and facts once known and recorded are easily overlooked or forgotten. In 1915, in the last of our series of papers on the cerebrospinal fluid and its pathway, a paper chiefly devoted to the calcareous and osseous deposits associated with a cellular hyperplasia of the arachnoid [11], we in turn put forward as novel precisely the same views Cleland had advanced fifty years before regarding the derivation of these tumours from the arachnoid cell clusters. Five years later, Mallory [17] re-advanced the same views, and designated the tumours with the histological aspects of which he was chiefly concerned, as *arachnoid fibroblastomas*. Weed in the same year, though more interested in the physiological rôle of the membrane as a fluid container, nevertheless presented a convincing series of pictures from the meninges of the cat, showing that the clusters of cells may range from a moderate hypertrophy to actual tumours, in which most of the characteristic degenerative changes of these growths, as met with in man, occur.

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[1] Others had observed these cell masses before Schmidt. They had possibly been seen long before by Rainey [20], who imagined them to be ganglionic structures which regulated the blood supply of the cerebral vessels. Fifteen years later Ludwig Meyer [18] [19] in a more accurate study of the meninges in cases of dementia referred to them as "epithelial granulations." Meyer recognized their relation to the arachnoid, noted the calcareous deposits which Virchow later named, and pointed out the relation of these cell clusters to the bodies of Pacchioni, which Luschka [16] a few years before had conclusively shown to be of arachnoid origin.

Multiple Cerebral Herniations.

There is another matter relating to the arachnoid villi, apart from their histological characteristics and their possible relation to tumours, which had engaged the attention of a few pathologists. In 1870, before the Würtzburger Medical Society, von Recklinghausen exhibited as a curiosity a brain from a case of cerebral tumour in which small bits of cerebral substance, projecting into minute openings of the dura, more especially over the temporal lobe, had been torn off in the course of its removal. These minute lesions he recognized as multiple hernias of the cerebral substance. They had been observed by others long before him, by Cruveilhier for example, but no particular significance had been attached to them.

The matter excited no great interest until twenty years later when Benecke [2] reported as a great rarity two further cases showing these herniations, which he attributed to pressure. He pointed out that nests of endothelial cells were invariably present somewhere on the surface of the minute cerebral protrusions, and this led him to recognize their relation to the Pacchionian granulations.

Though in 1901 four other cases were incidentally recorded by Blasius [6] from Benecke's laboratory, the first thorough study of these lesions was published in 1908 by S. Burt Wolbach [28] who had observed them in a series of cases in which there had been tension, not, however, always due to tumour. Wolbach emphasized what is important in our present connection that the herniations occur in the regions where the normal arachnoid villi abound, a fact which carries with it the implication that the dural venous sinuses and their main branches are to be found in the same situations. He showed, furthermore, as did Schmidt, that these are microscopic or what one might call potential Pacchionian granulations, and concluded that "the multiple hernias of cerebrum and cerebellum always enter the dura through fissures occupied by arachnoid villi."

Though Schmidt himself published nothing further on the subject of the *Zellzapfen*, his interest evidently did not lag, for at least two papers, bearing on these matters, appear to have emanated from his laboratory. The first of them by Sophie Wojno [27] was on this subject of cerebral herniations which she recognized as occurring in the villi: but she dwelt chiefly on the fact that they may be found in conditions unrelated to tumour and attributed them, it would seem, to defects in the pia subjacent to the villi, which thereby permit the herniations to take place.

It may be recalled that all but one of the twelve meningiomas Schmidt had described were small growths and accidental post-mortem findings. Nevertheless, even under these conditions he had observed some of these herniations, more especially in the middle cerebral fossa. Apparently, therefore, he and his pupil were on the look-out for some explanation for them other than tension. They consequently were regarded as "physiological" herniations rather than pressure phenomena, and were attributed by Wojno to leptomeningeal defects.

There is, it seems to me, a much more plausible explanation of the presence of these herniations when there is no demonstrable increase of intracranial tension—a matter indeed very difficult to gauge by post-mortem appearances alone. In view of what we now know of the ease with which the brain takes up fluid and becomes œdematous, there are probably few individuals who with advancing years escape from periods of increased intracranial tension due to one cause or another. These must be particularly common in association with arterio-vascular disorders, and it is easily conceivable that the arachnoid villi under these circumstances may not only become hypertrophied into visible Pacchionian granulations, but that actual herniations may occur and subsequently recede with the subsidence of the œdema. Even in the presence of tumour when intracranial pressure is relieved by withdrawal of cerebrospinal fluid, by the intravenous administration of hypertonic salt solution, or more permanently by a generous decompression, it is not unlikely that these minute hernias may become reduced just as may the large hernias which protrude through operative defects in the skull. An illustration of this in the process of taking place is shown in the accompanying figure (fig. 9). The condition came to light during the study of the meninges of a patient who had been operated upon over the cerebrum through an error in diagnosis, when in reality there was a cerebellar tumour with internal hydrocephalus and great tension. A cerebrospinal leak communicating with the ventricle occurred, and fatal meningitis was the result, but for the few days before death there was a complete release from the pre-existing supernormal tension; and at autopsy it was evident even to the naked eye that many of the large and multiple hernias which abounded were being withdrawn from their pockets in the arachnoid.

These minute herniations, as a matter of fact, are very commonly produced by long-continued states of increased pressure. That they project into and dilate pre-existing spaces there can be no doubt, and that these spaces communicate with the arachnoid is evident from the character of the cells lining them. What interests us chiefly at this time are the areas in which they are most commonly observed, since they betray the situations of the chief arachnoid villi and their associated cell-clusters. They abound, as might be surmised, along the major dural sinuses where the tentorium and falx unite with the dura over the cerebral and cerebellar convexities, but they are also to be found in the basal meninges, being especially common over the tips of the temporal lobes and in the region of the Gasserian ganglia, where they correspond likewise with the situation of the venous sinuses. They can be best studied in previously hardened brains removed with their

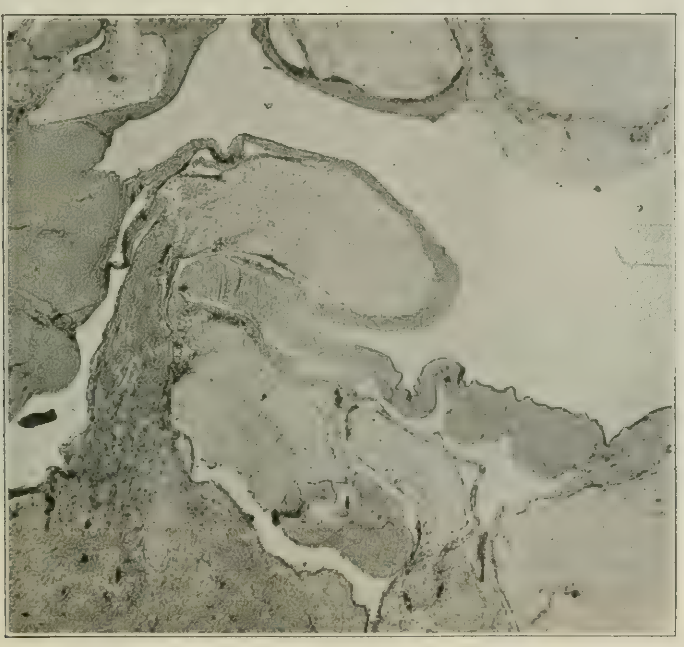

FIG. 9.—A cerebral hernia in the process of withdrawal from an arachnoid villus.

envelopes so far as possible intact; the accompanying figure (fig. 10), in which the relation of the protrusions to the branches of the vasa meningea media is apparent, gives an illustration of their distribution over the convexity.

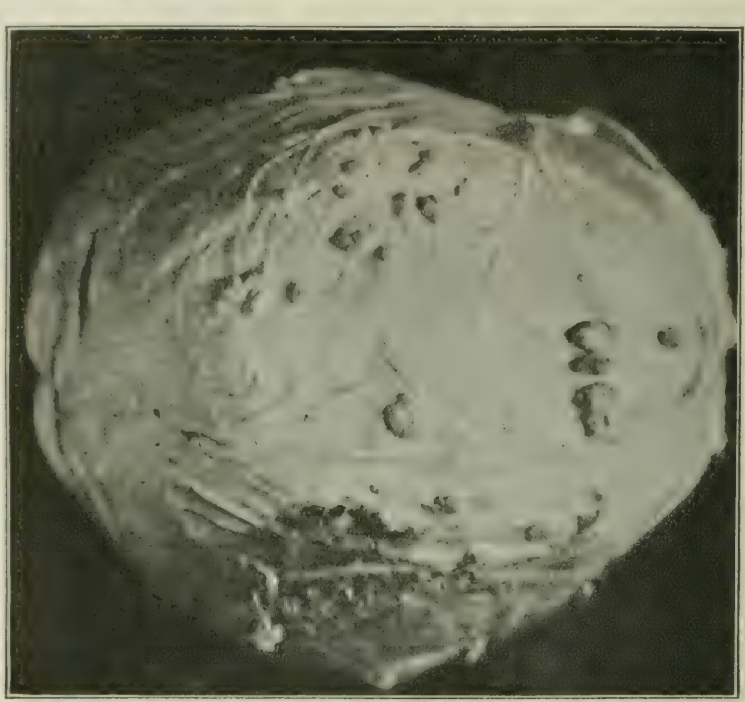

FIG. 10.—Showing multiple herniations, projecting through the dura over the left hemisphere, produced by pressure due to a large suprasellar endothelioma.

ÆTIOLOGY.

Why should these cell-clusters in the arachnoid have a tendency in middle life to undergo tumefaction? An answer to this question, owing to the many and wide gaps in our knowledge, must be essentially speculative. However, some approach to it can be made. As in other tumours, the more obvious factors are age, congenital predisposition, trauma and physiological activity. Schmidt's original observation that the cell-clusters are absent or difficult to demonstrate in infancy and become more pronounced with increasing age, has been confirmed by others. In this connection the age of the ninety-seven patients with meningiomas, as recorded at the time of their admission to hospital, fall in the successive decades as follows:—

0—10	0	50—60	21
10—20	3	60—70	10
20—30	11	70—80	0
30—40	23	80—90	1
40—50	28		

These figures naturally represent the age when symptoms had become pronounced, and probably an average of five or ten years should be subtracted if one were to estimate the age of onset. Nevertheless it can be seen that these tumours, unlike the gliomas, are rare in the first two decades, and reach their maximum in the fifth, a decade at least later than the period of maximal frequency for the pituitary adenomas and the acoustic tumours.

The fact that in cases of neurofibromatosis (Recklinghausen's disease), multiple meningiomas occasionally co-exist with multiple neuromas of the cranial nerves, suggests that some congenital fault may be responsible. However, they occur singly with far greater frequency. Curiously enough, they bear unmistakably a close relation to trauma of one sort or another[1]. In so many of the cases in the series has a tumour been found at the exact situation where a stunning blow had been received on the skull years before, that this must represent something more than mere coincidence. On the circumstantial evidence it is tempting to assume that the injury has bruised the meninges and caused an extravasation, to aid in the absorption of which the local cell-clusters have been incited into a state of morbid activity. It is not improbable, too, as emphasized by Borst, that some form of injury other than a blow may serve to incite a pachymeningeal reaction and lead to tumour growth. In one of the cases included in the series, an unsuspected frontal endothelioma was found post mortem associated with a subjacent chronic abscess. Moreover, psammomas and endotheliomas have been observed by Berger [3], Dufour [12], Henschen [15], and probably by others, in connection with old cases of healed spinal tuberculosis in which there were unmistakable evidences of pachymeningitis. Henschen, in particular, lays great stress on this relationship in reporting a case which showed multiple tumours. They have been observed, too, in association with pachymeningitis interna hæmorrhagica. In explanation of all this it must be borne in mind that the cells which line the arachnoid actually represent an organ of great functional potentialities. It is here that the studies of L. H. Weed and his co-workers have thrown a guiding light on the subject, for though an anatomist, Weed's interests have been on the side of function rather than structure.

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[1] The youngest case in the series, for example, a boy of 13, with a 100-grm. meningioma which originated from the lower margin of the falx, had had symptoms for five years. He had received at birth an extensive cranial injury, associated in all probability with a tear of the falciform membrane.

To state the matter briefly, the arachnoid villi in close association with which the cell-clusters abound, act as organic filters interposed in the pathway of the cerebrospinal fluid, between the subarachnoid spaces and the dural sinuses. Their non-development or their occlusion by foreign particles, whether the product of injury or disease, or suspensions of substances such as lamp-black introduced artificially into the cerebrospinal fluid, will lead to stasis of the fluid and hydrocephalus, provided the occlusions are sufficiently widespread [26].

Furthermore, the cell-clusters under the stimulus of these injuries are prone to hypertrophic enlargement. It has been shown by Essick [13] that when the villi are experimentally blocked by particulate matter, whether sterile or the product of inflammatory reaction, the arachnoid cells proliferate abundantly, take on the function of phagocytes, and even become free-moving macrophages in the subarachnoid spaces. We may regard these cells, therefore, as agents which play a rôle in keeping the points of outlet of the fluid free from the mechanical obstructions produced by debris.

It is conceivable, therefore, that with advancing years the mesothelial cells comprising the cell-clusters are called upon from time to time to undergo periods of increased functional activity in their phagocytic rôle, after which they remain permanently hypertrophic or subsequently undergo the characteristic and well-known degenerative changes to which they seem predisposed. Hence their apparent increase in size and number with advancing age. On the other hand, some of the cell-clusters, possibly in consequence of these periods of activation, show neoplastic tendencies under certain circumstances obscurely related to the genesis of tumour formation in general.

THE SITUATION OF THE TUMOURS.

It is evident from what has gone before, that at least four observers between 1864 and 1920 have independently come to the conclusion that these tumours, herein called meningiomas, are derived from the arachnoid cell-clusters. The relation of these groups of mesothelial cells to the functionating villi and of the villi to the dural venous sinuses, has been emphasized. It has been shown further that the places where the villi abound is indicated by the distribution of the minute cerebral hernias which protrude into them in cases of marked intracranial tension. It remains to be seen whether there is any definite correspondence between these regions and the points of origin of the tumours themselves.

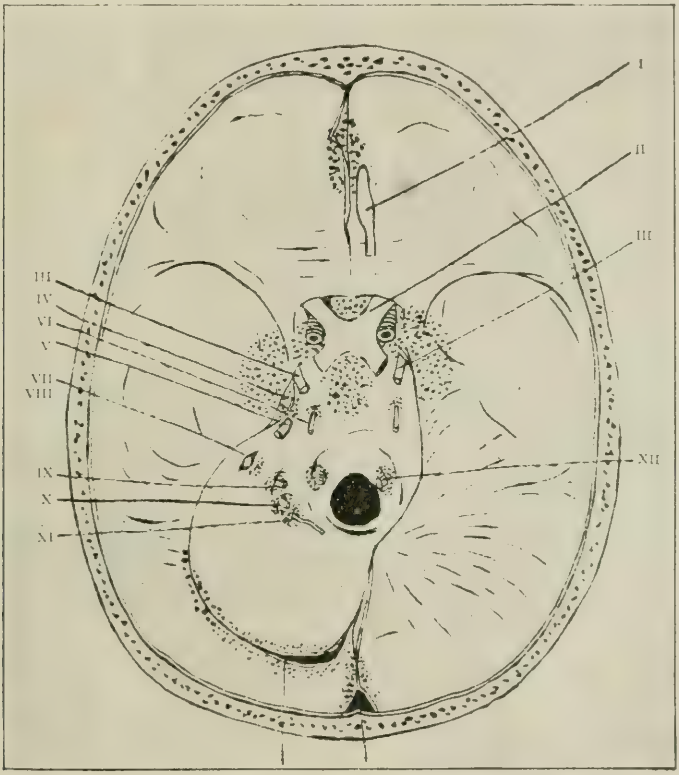

FIG. 11.—From Aoyagi and Kyuno, showing the situations of the cell clusters.

The only paper on this subject, to my knowledge, was published in 1912 by Aoyagi and Kyuno [1] and for a translation from the Japanese I am indebted to Professor Tanaka, of Okayama. These authors made studies of the dura of individuals of various ages to determine the seats of predilection of the arachnoid cell-clusters, and identified their presence in the following situations (fig. 11), viz., along the sinus sagittalis superior; near the crista galli; the sinus transversus; surrounding N. oculomotorius, trochlearis, abducens, and trigeminus; around the hypophysis; near the sella turcica; the plexus basilaris; at the point of penetration of the dura by the third, seventh, ninth, tenth, eleventh and twelfth cerebral nerves; and also at the points of penetration of the nerve-roots of the cervical spine.

Furthermore, they gathered from the literature thirty-six cases of so-called dural tumour (variously termed sarcoma, psammoma, endothelioma, sarcomatous endothelioma, spindle-cell sarcoma, &c.) and added three cases of their own, all evidently "meningiomas." The situations in which these thirty-nine tumours were reported corresponded sufficiently well with the principal locations of the cell-clusters to justify the conclusion that all the tumours—endotheliomas, psammomas and sarcomas alike—arose from these bodies.

For the purpose of this lecture, the accompanying drawings have been made, with as great accuracy as our records of operations and the study of autopsy material permits, to indicate the areas of dural attachment of the meningiomas in my personal series. It must be admitted that in certain cases it may be difficult, even with the material in one's hand, to judge of the exact point of origin of a meningioma. This is particularly true of the spreading flat tumours[1], for such a small stalk of attachment as appears in the case herein recorded in some detail (figs. 2 and 3) is unusual even in the large potato-like growths which tend to be more or less pedunculated.

The meningiomas, in short, may be divided into two general classes: the large growths, often more or less irregularly lobulated, which incline on the whole toward a spherical form, and the tumours *en plaque* which are but slightly elevated and tend to spread over the inner dural surface. These latter meningiomas represent but a small proportion of the tumours in the series, and without the microscope would hardly be recognized as belonging to the same general group. They are more common among the growths arising from the basal meninges than from the convexity, though three of them occupied the parasagittal angle and a number have been found spreading over the dura in the sphenotemporal region. In this latter situation they appear to arise from near the pterion, where the meningeal vessels and sinuses so commonly channel the bone. Though these meningiomas *en plaque* are but slightly elevated and resemble a granulomatous meningitis rather than a new growth, they are particularly prone to push through the dura and to invade the overlying bone.

This tendency of the meningiomas to provoke a cranial hyperostosis constitutes a story by itself, and it must suffice to say that a considerable percentage of all these tumours produce a marked effect on the adjacent bone. There may be a very slight involvement of the inner table (as in fig. 1), or a marked endostosis corresponding approximately to the centre of the area of dural attachment which is indented thereby. Occasionally the bone is enormously thickened over the growth, as much as three or four centimetres in extreme cases, and under these circumstances the canaliculi are filled more or less extensively by tumour cells, which in time may replace the thickened bone by a core of solid tumour. These characteristics are schematically shown in the accompanying drawings (fig. 12), and they are mentioned because the photographs, X-rays and measurements giving the situation of these hyperostoses have been an additional help in placing the situation of a number of the tumours in the series. There are other ways by which the location of the seat of origin may be identified with fair accuracy, though chief reliance has been placed on the sketches and diagrams of the operations which accompany the old case records.

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[1] An example of one of these lesions, which are particularly apt to be associated with an overlying hyperostosis cranei, has been recently reported in another connection [9].

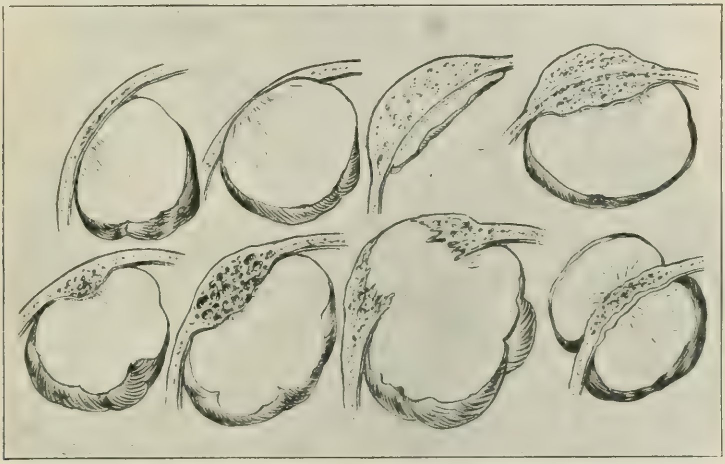

FIG. 12.—Diagrams of the various ways in which the meningiomas affect the overlying bone.

With due allowances, the plotted charts (figs 13 to 16) are sufficiently dependable. Though self-explanatory, there are certain features to which attention may be called. It is evident that the lesions are more numerous in the frontal regions, both of the vault and base, so that the frontal lobes have been involved through deformation far more often than any other part of the brain. Many years ago attention was called by Blackburn [5] to the fact that frontal endotheliomas are a not infrequent post-mortem finding in those who have died in asylums, but until these diagrams were made I would not have believed that the tumours in our surgical series would, on the whole, have tended to be so far forward.

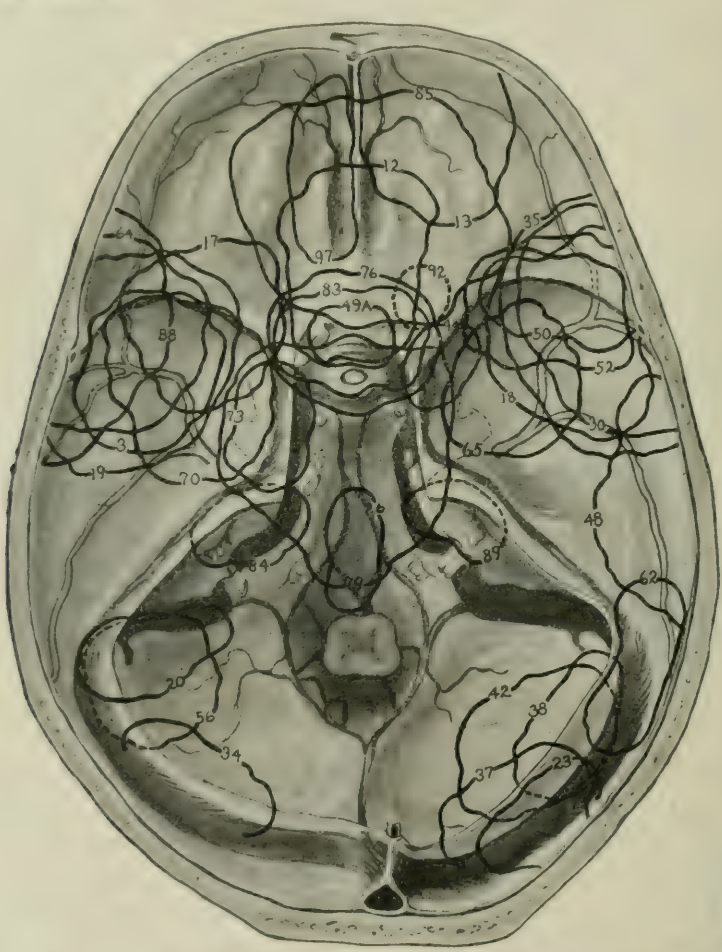

FIG. 13.—To show the areas of dural attachment of the meningiomas in the series in their relation to the major sinuses of the basal meninges.

Unquestionably many of these lesions are never recognized during life, and even if a diagnosis of "tumour suspect" actually be made, the localization of the lesion may be extremely difficult in the absence of an area of hyperostosis, either palpable or shown by X-rays. It is possible, therefore, that the blank areas in the diagrams merely repre-

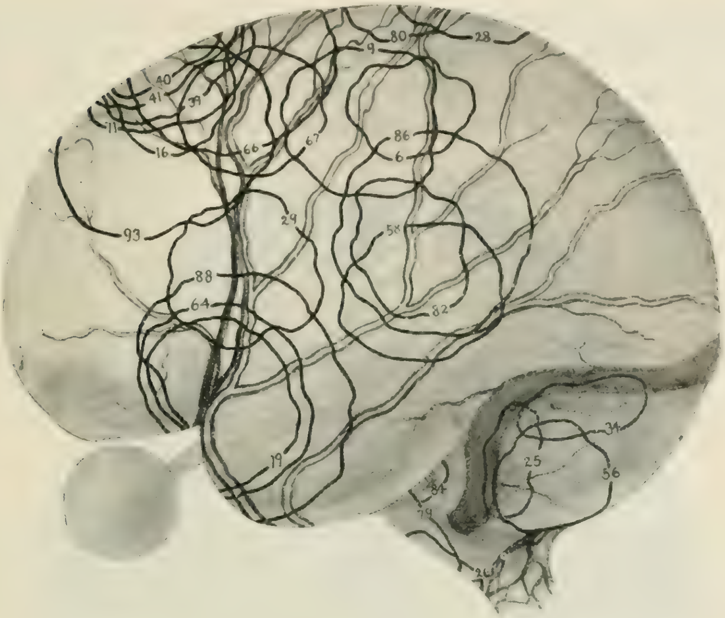

FIG. 14.—To show areas of dural attachment of the meningiomas and their relation to the dural sinuses on the left lateral aspect of the brain.

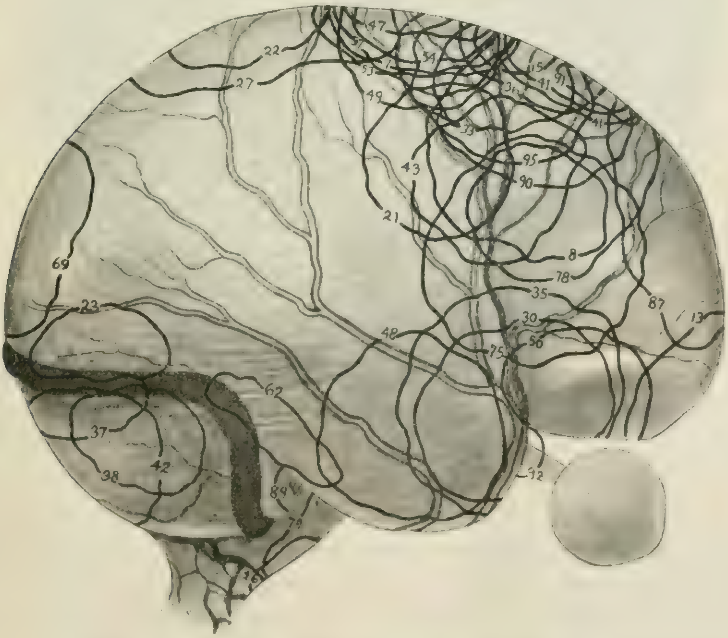

FIG. 15.—To show areas of dural attachment of the meningiomas and their relation to the dural sinuses of the right lateral aspect of the brain.

sent relatively silent fields in which tumours are less likely to have been recognized clinically. One point in favour of this is the fact that the recorded tumours show a wider distribution over the left than over the right hemisphere. The single example of tumour far posterior on the convexity of the right hemisphere (No. 27, fig. 19) was a purely accidental post-mortem finding. The patient was an acromegalic with a primary optic atrophy and homonymous hemianopsia attributed to a pituitary adenoma, and owing to the combination of his profound psychosis and an inaccurate clinical history he passed through our

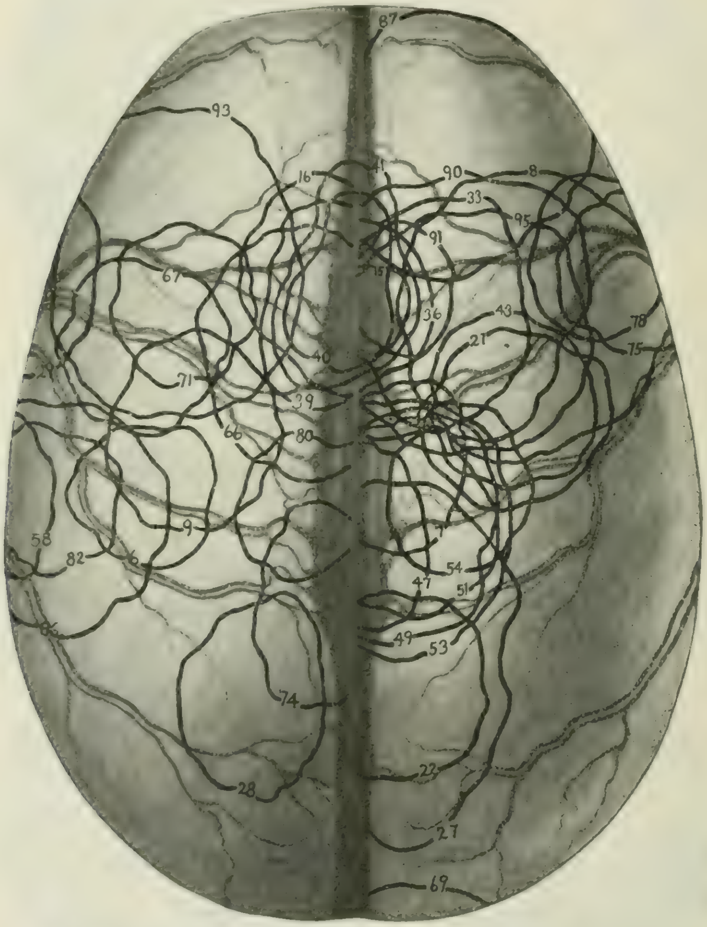

FIG. 16.—Superior view of the meninges, showing the tendency to an anterior disposition of the tumours, and the prevalence of their origin from the lateral expansion of the sinus sagittalis.

hands with the meningioma unsuspected. He died a year later in an asylum, where at autopsy a large parasagittal meningioma (fig. 17) was unexpectedly disclosed.

Mere diagnostic oversight, however, cannot alone explain the predominance of anterior lesions, for notably in the posterior fossa under the tentorium, where localization should be easy, meningiomas are particularly rare. This is true, also, of the growths involving the occipital lobe, of which there have been only three in the series, whereas on the other hand the extraordinary prevalence of tumours which take their origin from the meninges of the suprasellar region and cribriform plates of the ethmoid cannot be accounted for on the basis of chance alone.

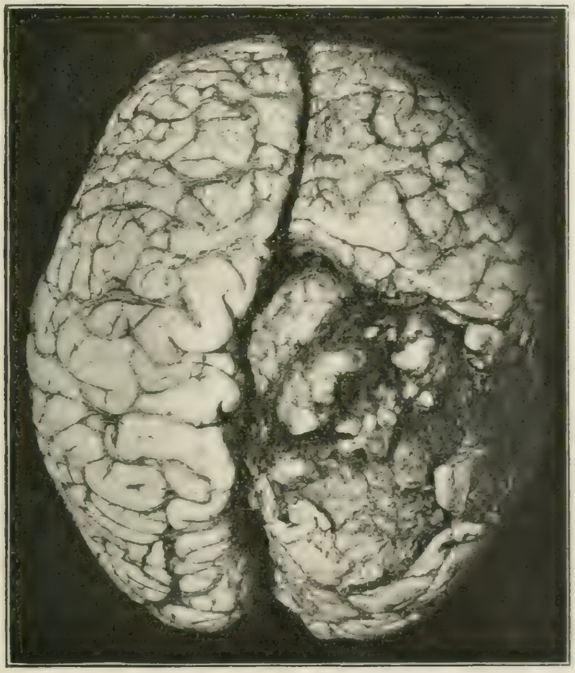

FIG. 17.

I have spoken of the three ways of approaching the study of a large series of tumours and, so far, have refrained from any discussion of the meningiomas according to their locality. The endeavour has been made with no great success to subdivide them for working purposes into several clinical groups. These may deserve a brief mention.

(1) *The spinal meningiomas.*—These occur at different levels of the cord, and judging from my small series of twelve cases in which the greater number are midthoracic, they arise more often from upper than lower areas of the spinal theca. They are well-known lesions, frequently operated upon with success since 1888, when Horsley and Gowers so brilliantly led the way. What, however, is not commonly recognized, or at least emphasized, is the fact that they take their origin from the arachnoid at the point of emergence of one of the nerve-roots, so that the growth usually lies at the side of the cord, and is overlain by the nerve-root in question. This explains the characteristic discomforts of these cases, and the frequent tendency to a Brown-Séquard type of spinal palsy.

(2) *The cranial-nerve foraminal tumours.*—These cases fall into three groups, though they may be capable of greater subdivision since the cell-clusters from which they arise are said to exist at the foramina of exit of all the nerves. The tumours we have encountered have arisen (*a*) at the porus acusticus with loss of hearing as the inaugural symptom, suggesting an acoustic neurinoma (1 case); (*b*) from the trigeminal sheath, a common seat of origin, with trigeminal pain and hypæsthesia as early symptoms (5 cases); and (*c*) in the orbit itself, from the arachnoid sheath of the optic nerve, producing a unilateral painless exophthalmos (1 case).

A peculiarity of the basilar tumours, particularly those of the trigeminal region, is that they may spread widely in the basal meninges and become thereby irremovable. This, however, is not invariable, for one tumour (No 26) in the series which arose from the dura over the basilar process just within the foramen magnum, was egg-shaped with a small stalk of attachment.

(3) *The suprasellar tumours.*—These are fairly common, the series containing eight examples. The tumours arise from the meninges covering the Willisian circle of sinuses surrounding the pituitary diaphragm. Except for the fact that they occur in adults, whereas the suprasellar tumours originating from the cranio-pharyngeal pouch (Rathke) usually give symptoms in childhood, the manifestations of the tumours of the two types are very similar, consisting chiefly of primary optic atrophy, of field distortions often with hemianopsia, and finally of secondary dyspituitarism.

The growths may project upward into the region of the third ventricle, and may reach an enormous size. As several of them have been unexpectedly encountered at operations conducted for presumed pituitary tumours, they have merely been verified by the removal of a small fragment of tissue and, except in one instance where a small, easily dislodged tumour was found, no attempt has been made to extirpate them. Consequently, except for the two cases encountered at autopsy, both of which show a remarkable similarity, the exact delimitations of the areas of attachment are somewhat conjectural.[1]

(4) *Tumours arising from the olfactory groove of the ethmoid.*—In Cruveilhier's plate one of these characteristic growths is pictured, and the later literature contains reports of many others in the same situation. Though more anterior than those just referred to as suprasellar, the growths have very much the same appearance. They are exceedingly difficult to diagnose. Occasionally a fortunate stereoscopic X-ray may show some local bone absorption and unexpectedly reveal the situation of the lesion, but otherwise there may be nothing more than some obscure mental derangement possibly with anosmia until the growth extending backward reaches a sufficient size to press upon one or both optic nerves. The tumour may be median and separate the two frontal lobes widely, or, if unilateral as in the single case in the series in which a total extirpation was successfully accomplished, it may press upon the homolateral optic nerve and give a primary atrophy, whereas the opposite eye shows a choked disc.

(5) *Sphenoidal ridge tumours.*—The growths which lie astride the sphenoidal ridge, with a portion of the tumour resting on the orbital plate under the frontal lobe and a portion in the middle fossa indenting the temporal lobe, are fairly common and characteristic. Most of them have been unexpected findings, though one or two have been recognized because of an absorption of the sphenoidal ridge shown by an antero-posterior röntgenogram. They may cause uncinate seizures and not infrequently encroach on the side of the chiasma and produce an homonymous hemianopsia.

(6) *Sylvian cleft tumours* (*temporo-frontal*).—These are, on the whole, similar to the above and doubtless arises from the same sinus, but they lie sufficiently far lateralwards to be brought into view by a subtemporal decompression. Two of them which gave no localizing symptoms were unexpectedly disclosed in this way and were subsequently removed by an osteoplastic exposure. In this region, too, for some unexplained reason, the tumours *en plaque* are common, and as these meningiomas are apt to provoke hyperostosis and cause a palpable thickening of bone at the temporo-sphenoidal junction, they are easily

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[1] One of these cases was fully recorded because of its pituitary manifestations in my monograph, "The Pituitary Body and its Disorders," 1912, Case No. viii, pp. 63-72.

recognized through this indication of their presence, as well as by the marked exophthalmos which occurs if the hyperostosis involves the outer orbital wall.

(7) *Tumours of the convexities.*—These, twenty-eight in number, naturally represent a large proportion of any surgical series. They are not only easily accessible, but when they encroach on the sensori-motor cortex, characteristic and well-known symptoms of definitely localizing value are often produced. For this reason, small surface meningiomas which cause Jacksonian seizures followed in time by palsy not uncommonly fall to the lot of the general surgeon.

The tumours arise from arachnoid cell-clusters in connection with the spheno-parietal sinus and the vasa meningea media. They may be subdivided into *temporal*, *frontal*, *paracentral*, *parietal* and *occipital* tumours, and the diagrams show that in spreading up from the last described group which centres around the Sylvian notch, they dispose themselves in some correspondence with the fan-shaped distribution of the sinusoidal veins of the dura. They predominate over the frontal areas and their points of origin may be found even as far forward as the tip of the lobe. The series contains no examples of tumours arising over the posterior surfaces of the hemispheres except those which take origin from the major sinuses. They are included in the following groups:—

(8) *The parasagittal meningiomas.*—These, in a way, are the most interesting and characteristic of all. The case (No. 15) selected as a text for this lecture was of this type, and the series contains twenty-six other examples. The tumours arise from the wall of the sinus or its lateral expansion, and are apt to have some attachment to the surface of the falx as well. Consequently, as the growth enlarges, the mesial edge of the hemisphere gets pushed away to a greater or less extent from the parasagittal angle.

When a parasagittal tumour is surmounted by a dome of hyperostosis, its situation and identity are easily recognized. Also when Jacksonian seizures originating in a foot are followed in the course of years by a spastic paralysis which begins in the corresponding leg, one may feel reasonably assured that a parasagittal meningioma will be disclosed at operation, provided the mesial edge of the hemisphere can be brought into view.

When, on the other hand, the parasagittal tumours arise well in front of the motor cortex or, what is less common, posterior to it, they may be exceedingly difficult to localize by symptoms alone. An example of this has already been cited in connection with Case 27 (fig. 17). There have been only two tumours in the series deforming exclusively the occipital lobe. One of them (No. 69, figs. 15-16), a parasagittal tumour originating near the tentorial angle, was successfully enucleated with perfect recovery. The other, a huge 200-grm. tumour not represented in the diagram as its point of origin remains obscure, was incompletely removed, and there was a continuance of the growth with fatality at a secondary operation some years later.

(9) *The meningiomas of the falx.*—No mid-line diagrams permitting the representation of these tumours have been made, for the series contains only two examples. Both of them were large tumours of almost spherical form, with the smallest possible area of attachment at the lower margin of the falx. Their presence in each case was identified by exploratory punctures, and both were removed by transcortical incisions with death in one case and recovery in the other.

This I cannot believe represents fully the true percentage of tumours originating from the sides of the falx, for bony plaques and endotheliomatous patches, as is well known, are not uncommonly found there in the ordinary run of post-mortem examinations on old people.

(10) *Tumours of the sinus transversus and sigmoideus.*—The series contains only two supra-tentorial tumours of this origin (Nos. 62 and 23, fig. 15). One which gave no localizing symptoms was first unexpectedly exposed during a right subtemporal decompressive operation. Its comparatively small attachment corresponded to the knee of the sigmoid sinus. One other (No. 23) was farther posterior, a large tumour which had caused a hemianopsia.

On the other hand, there have been five subtentorial tumours giving a cerebellar syndrome. All of them arose from the lower wall of the transverse sinus, and all were successfully removed at operation. I confess to some surprise that these growths are not more common in this situation, in view of the abundance of arachnoid villi which project into the subtentorial wall of this sinus and which all surgeons familiar with cerebellar explorations have been accustomed to observe.

These, then, are the chief topographical subdivisions into which the tumours have been tentatively grouped for clinical purposes. Doubtless some far better regional classification will be made as the particular symptom-complex called forth by a growth in these several regions comes to be more clearly understood. Certain of them, like the parasagittal tumours which impinge on the motor cortex, can with a fair degree of diagnostic accuracy be foretold before operation, but in the absence of an accompanying hyperostosis most of the others are as yet chance findings in the course of an exploration, though a long history of slowly advancing trouble may make one suspect the presence of a meningioma.

I hope some day, using this lecture as a basis, to give the detailed report of the individual cases in this series with their triumphs as well as their tragedies. Our experience may be summarized as follows: (1) A few of these tumours have been accidental post-mortem findings in patients in whom brain tumour was unsuspected; (2) three of them have been late post-mortem findings in patients who had been operated upon some years before for presumed tumour, but as this procedure revealed neither tumour nor tension the cases had been variously diagnosed as some condition other than tumour; (3) in some of the cases (possibly ten) the growth, which produced no localizing symptoms, was accidentally disclosed during the course of a subtemporal decompression; (4) in the majority of the cases the presence of a tumour was obvious and its location definite, but there is no pre-operative statement in the case history to show that its nature was anticipated; (5) in a few of the operated cases not only was the location of the tumour evident, but a presumptive diagnosis was made of its character. This, of course, applies to all tumours with hyperostosis, as well as to several trigeminal, suprasellar and parasagittal lesions without osseous changes. Naturally, if one makes a diagnosis of meningioma in all patients with symptoms of brain tumour, he will be correct in about 10 per cent. of his cases, but we should aspire to something far better than this low figure.

The foregoing rough subdivision is made in order to encourage others and to spur ourselves in an effort to enlarge the percentage of cases falling in the last group. Certainly, with our present knowledge of these lesions we should to-day with a corresponding group of cases be able to make a correct pre-operative diagnosis in at least half of them. Small tumours such as those described by Schmidt as accidental post-mortem findings give no recognizable symptoms and have no surgical bearing unless they happen to impinge upon some important cortical area and provoke Jacksonian seizures. But the larger tumours, even when in silent areas, ought to be capable of recognition if chronology and duration of symptoms, age of patient, extracranial circulatory signs and the frequent hyperostoses are taken into account. Accordingly, it should be possible in an ever increasing percentage of cases to foretell not only the situation of the growth, but to anticipate its character as well. This, in an operation so elaborate as one for brain tumour, is an enormous advantage.

There is no gainsaying that despite the enucleability of these tumours when they are easily accessible the operations are often attended with great hazard, and more often than in the case of other tumours this must be done in two or even three sessions. One reason for this is that before its presence has been even suspected, the growth may have attained a large size, and by venous stasis have greatly increased the vascularity of scalp and bone.

There is to-day nothing in the whole realm of surgery more gratifying than the successful removal of a meningioma with subsequent perfect functional recovery, especially should a correct pathological diagnosis have been previously made. The difficulties are admittedly great, sometimes insurmountable, and though the disappointments still are many, another generation of neurological surgeons will unquestionably see them largely overcome.

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NOTICES OF RECENT PUBLICATIONS.

The Mechanism of the Brain and the Function of the Frontal Lobes. By Professor LEONARDO BIANCHI. Authorized translation from the Italian by James H. Macdonald. Pp. 384. Edinburgh: E. and S. Livingstone. 1922. Price 21s. net.

Professor's Bianchi's views on the functions of the frontal lobe are based on numerous experiments on the brains of animals, chiefly monkeys, carried out over a long period of time. Interpreting the results of these experiments in the light of his study of the evolution and structure of the frontal lobes and of the pathways connecting them with the rest of the brain, as well as the various doctrines of neuro-physiology to which that study gives rise, Bianchi is convinced that in man these lobes are specially concerned in the synthesis and elaboration of the higher intellectual and sentimental processes, and all the various attributes of sociality. They play a most important part, he holds, in the formation of the psychic personality, and the development of the powers of conscious volitional behaviour.

Professor Bianchi divides the cerebral cortex into two main evolutionary levels, the postfrontal motor and sensory areas, and a prefrontal area that is neither motor nor sensory; he also postulates two grades of psychic activity, a "lower" and a "higher" consciousness, resulting from the activity of these two levels. In the lower or postfrontal consciousness, only the simplest mental constructions obtain; life is centred around sensations, desires, and instincts; conduct is impulsive and egoistic, and tends to the immediate satisfaction of individual needs only. In the higher or prefrontal consciousness, reason and all the potentialities of thought come into play; and impulses become subject to voluntary inhibition and control and are influenced by factors arising from the development of the more lofty sentiments and the higher social tendencies and obligations. When Bianchi speaks of the higher consciousness as prefrontal he does so only in the sense that it is the prefrontal area of the cortex that contributes to it its most weighty factors. Its centre of centres is in the prefrontal area, but it is necessarily open, he maintains, to currents from all parts of the cerebral mantle, and it thus comes to form with the lower consciousness a wide network of ideas and experiences which embrace the products of all the cortical centres. That power of starting, directing, evoking and selecting the nervous currents, possessed in a minor degree by all the cell-groups of the cortex, belongs in supreme part to the prefrontal area. In Bianchi's view, therefore, the frontal lobes are the seat of the final synthesis and fusion of the incoming and outgoing products of the several sensory and motor areas of the brain.

The work of the brain, as a whole, is carried on by processes occurring in different levels of physiological complexity, the later and more highly evolved areas assimilating, synthesizing, and modifying the products of other lower subsidiary levels, and in dealing with the highly complex psychical end-products of prefrontal synthesis. Bianchi sees no reason for treating them differently from the other products of cerebral activity of a more physical character, or thinking that their governance is by laws in any essential way different from those that obtain in the more purely physiological sphere. He discusses the results of frontal lobe activity, therefore, wholly as biological products, not as spiritualistic or metaphysical abstractions, and in doing so necessarily lays the greatest stress on the multitudinous combinations of innumerable lesser grade compounds in their final elaboration. What it involved in the last analysis, in the psychic transmutation or "mentalization" of matter, may be still open to conjecture, but even here Bianchi offers some suggestive speculations in regard to the light which the study of the behaviour of electrons may throw on the subject.

Professor Bianchi's opinions concerning the function and relationship of the different parts of the brain, founded as they are on the results of extensive experimental investigations, must command our respect, while his careful attempt to evaluate psychic phenomena on a biological basis affords us no slight glimpse into the mechanism of the brain's activity, and serves as a stimulating corrective to those aspects of psychological thought which tend to divorce mental processes from their physical substratum. His insistence too, at the end of his book, on the primary importance of rightly trained, conscious intention and intelligence in the conduct of the practical affairs of life is especially valuable at a time when, too often, the "urge" of the unconscious is apt to be used as an excuse for the lack of that self-control and sense of responsibility, for the cultivation of which he pleads. He expresses "grave doubts" indeed, of the automatism of the unconscious, apart from any directive effect due to the action of the conscious will.

A word in conclusion must be said about the translation of this book. Dr. Macdonald has done this in a way that cannot be too highly praised, and has given us a scholarly English version, in all respects worthy of its distinguished author.

Questions neurologiques d'actualité. Pp. 551. Paris : Masson et Cie. 1922. Price 28 francs.

In this volume there are collected together twenty lectures on neurological subjects of special interest delivered before the Faculté de Médecine de Paris in 1921. Each of the lecturers was free to choose the subject that appeared to him of most importance at the moment, and each subject selected has been consequently dealt with by one capable of placing before his audience views of an authoritative and reliable nature.

In most cases the aim of the lecturer has evidently been to put forward the observations and opinions on his subject that appeared at the moment most trustworthy rather than his own personal views, but many of the articles show evidence of original investigation and research. In some instances, however, the lectures are based on the original investigations of the authors; this is particularly so in Kinnier Wilson's contribution on the pathogenesis and pathological physiology of progressive lenticular degeneration, and in Pierre Marie's discussion of the question whether preformed and innate centres for speech exist in man. In both of these, as well as in Claude's paper on intracranial hypertension and serous meningitis and in Lhermitte's on lethargic encephalitis, in which the subject matter consists mainly of original work already published, we are fortunately provided with the views these neurologists hold to-day after reviewing their earlier work in the light of further experience and criticism. A few of the lectures on the other hand merely represent the ordinary teaching of the day, without any analysis or critical selection of facts and hypotheses.

There are, however, few of these lectures which will not repay perusal by any neurologist, and all will be valuable to the general physician and even to those specialists who are unable to keep pace with the neurological literature.

The only serious fault that can be found with the volume is absence in almost all the articles of bibliographic references to the work of others which is cited.

Report of the War Office Committee of Enquiry into "Shell Shock."
H.M. Stationery Office. 1922. Price 6s.

The reference to the Committee was to collate the expert knowledge derived by the Naval and Military Authorities and the medical profession from the experience of the war with a view to recording for future use the ascertained facts as to the origin, nature and remedial treatment of "shell shock," and as to whether by military training or education some scientific method of guarding against its occurrence could not be devised.

In a brief note on this report, it is scarcely necessary to enter into a consideration of the more purely military aspect of this subject, but a summary of the medical findings may not be without interest.

It was agreed that "shell shock" had been a gross and costly misnomer, and that the term should be eliminated from the nomenclature. The war produced no new nervous disorders, all those which occurred had previously been recognized in civilian practice. Owing to the special circumstances of the war these disorders appeared in some cases in an aggravated form, and the numbers suffering from them were very large.

The cases divided themselves into three main groups: genuine concussion without visible wound; emotional shock, either acute or developing slowly as a result of prolonged strain and terrifying experience, the final breakdown being sometimes brought about by some relatively trivial cause; and nervous and mental exhaustion the result of prolonged strain and hardship. In many cases, however, the three factors of commotional and emotional shock and exhaustion were combined in varying proportions.

Many points of interest have been brought to light and the verbatim evidence of witnesses is by no means the least instructive part of the report. Here will be observed personal experiences bearing upon the psychology of fear, upon cowardice, upon malingering, upon the influence of war stress in the production of insanity, and valuable recommendations upon the prevention of "shell shock."

The treatment of the neuroses observed in soldiers is considered in detail, and the several forms of psychotherapy are commented upon with fairness and discretion.

The report may have a much wider significance than was intended when the idea of an inquiry was broached, as it deals with psychological problems which are not confined to war conditions.

Remembering and Forgetting. By T. H. Pear. Methuen. Price 7s. 6d.

The analysis of dreams has been described as the royal road to the understanding of the unconscious. If we broaden the issue by substituting memory for dreams we will find that it becomes the nuclear problem of modern psychology, the full appreciation of which can only be obtained by the analysis of Memory and Forgetting.

This is the task that Professor Pear has undertaken in his book, designed primarily for the interested layman and the medical man who is interested in the psychological problems of medicine.

Being engaged in the elucidation of the experimental and theoretical problems of normal psychology, Professor Pear has not approached the subject in the manner of the psycho-analyst—that, is by plunging directly into the concrete details of the mental life—but begins by an analysis of memory processes from their genesis at the perceptional level, to the formation of after-sensations; thence to visual, auditory and kinæsthetic imagery, and ultimately to the formation of generic images upon which our ideas are based. This prepares the way for a consideration of the dream-life. The Freudian conception is fully considered, as well as the additions to it made by Rivers. He ends his analysis by a chapter on forgetting, which in the light of modern theory is the justification of all the preceding chapters.

There are one or two features of the author's method which make his treatment of the subject somewhat insufficient. Firstly, his own annoying visual imagery makes the subject appear easier than it actually is, although he does not fail to emphasize the importance of kinæsthetic imagery; and secondly the insufficient stress laid in the earlier chapters on dreams on the affective tone of the memories in dreams.

The two essays on synæsthesia and number forms are important for the psychology of imagery, and have an indirect bearing on the subject of remembering.

The whole book would well repay reading even to those engaged in applied psychology, for it deals with the theoretical basis of memory. It is written in a clear and succinct style.

Suggestion and Mental Analysis. By WILLIAM BROWN. Pp. 165. University of London Press. 1922. Price 3s. 6d.

The author is of the opinion that the two main forms of psychotherapy, that is suggestion and mental analysis, are not mutually exclusive as the extreme partisans of each system maintain. The aim of this small book is to give an elementary and non-technical account of their relations to one another, and to show that by harmonizing them as far as possible a sound system of psychotherapy can be built up.

The earlier chapters form a concise and in the main a sufficient introduction to the subject for the layman and non-specialist for whom the book is written, while the last three deal chiefly with Bergson's philosophy and the relation it bears to the author's own views.

Though written in a simple and clear style the book lacks the cohesion so necessary in an elementary text-book.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

[December, 1922.]

BRAIN.

PARTS 3 and 4, VOL. 45.

TWO CASES OF SYRINGOMYELIA AND SYRINGOBULBIA, OBSERVED CLINICALLY OVER MANY YEARS, AND EXAMINED PATHOLOGICALLY.

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AND

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Syringomyelia, although perhaps not so unusual as at one time it was supposed to be, is a very interesting disease, because of the clear association which it is possible to trace between the anatomical change in the spinal cord and bulb, and the clinical condition. The two cases which we are about to relate are perhaps unusual because of the long periods during which it was possible to observe them carefully. They also have a special interest because of the striking manner in which the clinical course differed in the two cases. In the first patient the condition underwent no change of consequence during the long period of twenty-four years in which one of us (J. T.) had him under almost continuous observation; in the second, who was also under observation for a long period, viz., nineteen years, there was on the contrary a slow but steady deterioration in the physical condition determined by the gradual spread of muscular weakness and sensory change, the result no doubt of corresponding changes in the condition of the spinal cord. The detailed description of the morbid changes in the spinal cords, for which two of us (J. G. G. and J. P. M.) are responsible, explains to some extent this difference.

H. M., a pastrycook by occupation, was admitted to the National Hospital, Queen Square, under Dr. Hughlings Jackson on May 15, 1893. He was at this time 23 years of age and had previously been under Dr. Jackson's care at the London Hospital. He said that four and a half years before admission he had experienced pain in the right occipital region, with numbness in the arms. Three months later there developed squinting of the right eye and diplopia, and a few days later there was numbness of the right side of the face and complete loss of sensation here which lasted for a fortnight. This, he said, had since practically cleared up. Four days after experiencing numbness of the face he noticed that the right side of the face was motionless, and he stated his articulation was indistinct and the tongue on protrusion went to the right. For the last four months before admission the occipital pain had been worse, and there was tingling and loss of feeling down the right arm and leg.

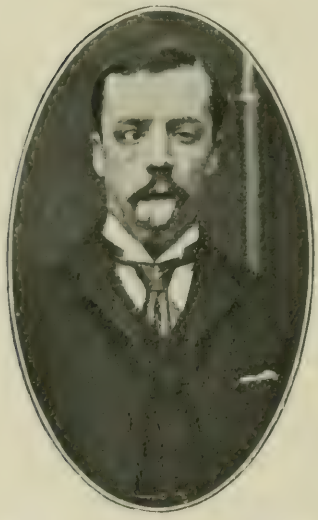


FIG. 1.—Case I. Patient in 1893.

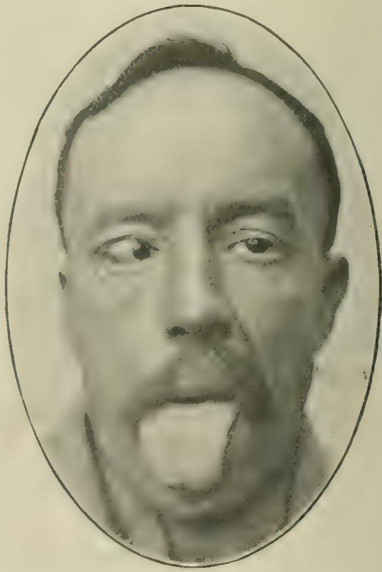


FIG. 2.—Case I. Patient in 1915.

There was nothing of significance in his family history or in his personal history. He had had no serious illness and he denied venereal disease.

On admission he was found to have a marked right internal strabismus due to complete paralysis of the right sixth nerve. There was also complete facial paralysis on the same side and the tongue protruded to the right. The right side of the tongue was much wasted, and although the temporal and masseter muscles on both sides were strong and active, the jaw dropped to the left when the mouth was widely opened. There was a good deal of wasting about the shoulders, more marked on the right side, and although the trapezius and other

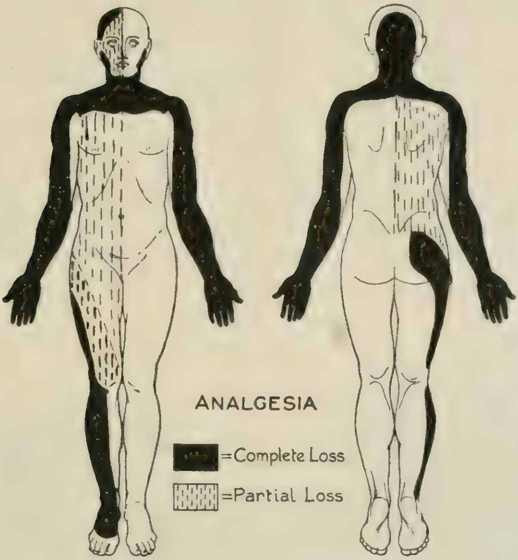


FIG. 3A.—Case I. Analgesia in 1893.

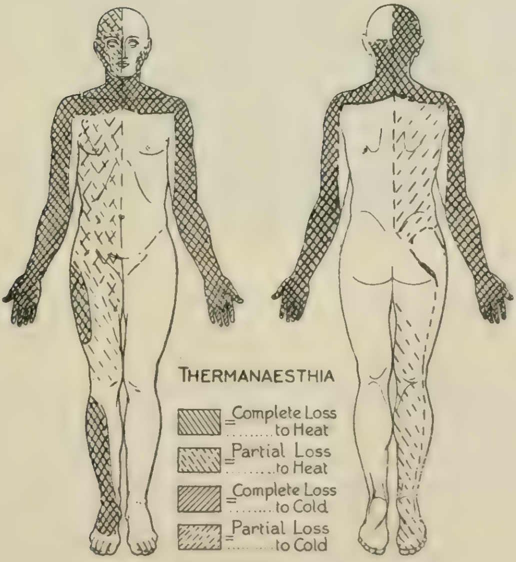


FIG. 3B.—Case I. Thermanæsthesia in 1893.

muscles of the shoulder-girdle all responded to a faradic current on this side, a stronger current had to be used than was sufficient to produce a good contraction on the other side. There was no wasting of the lower limbs: the knee jerks were present and there was no ankle clonus.

The sensory changes were very distinct and interesting. They are so graphically represented in the accompanying diagrams that no further description seems called for. (Figs. 3A, B and C.)

The diagnosis in this case was not difficult, and although at that time—1893—we were not very familiar with syringomyelia, there was no hesitation in concluding that this was a case of that nature. It was apparent that the morbid process had affected not only the spinal cord, especially in its cervical portion, but had also spread upwards so as to involve bulbar and pontine structures, as was shown in the wasting of the tongue, the facial paralysis, and the paralysis of the sixth nerve on the right side. The sensory changes also indicated involvement of the fifth nerve or its nucleus.

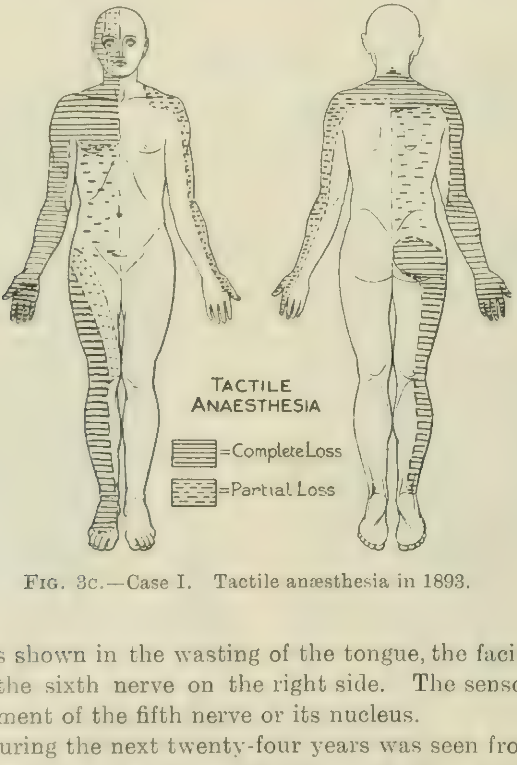


FIG. 3C.—Case I. Tactile anæsthesia in 1893.

The patient during the next twenty-four years was seen from time to time and examined carefully, but no material change developed. He enjoyed fair health, although he complained a good deal from time to time of pains in his head and limbs. He married but had the misfortune to lose his wife in 1916 and became very much depressed. He committed suicide by hanging in the following year, having previously asked his brother-in-law to communicate with one of us (J. T.) if anything happened to him. Through the kindness of the Coroner a post-mortem examination was allowed, but as this was not carried out until forty-eight hours after death the sections of the cord were not as good as they might have been had it been possible to make the examination earlier. It will be seen that the examination confirmed the diagnosis.

CASE I.—PATHOLOGICAL EXAMINATION.

The brain and cord were fixed directly in Müller's fluid, where they remained for over a year. In consequence of this, permanent flexures had taken place at some segments of the cord and the tissue was rather brittle, so that it was impossible to avoid some distortion of the sections. The chief characteristics of the cord at each level could, however, be made out fairly well.

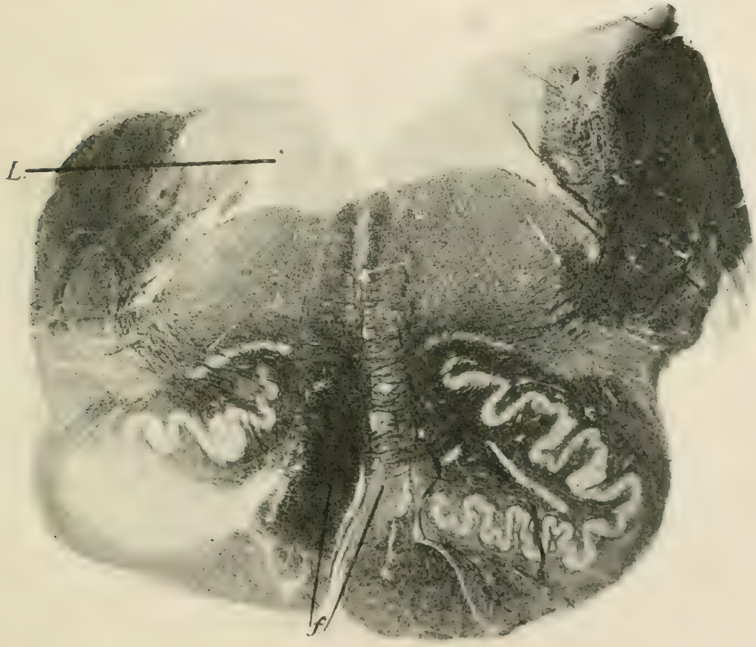


FIG. 4A.—Medulla near the lower end of the fourth ventricle. *f.*, Mesial fillet; *L.*, lateral extension of the cavity.

The process of gliosis and cavitation extended from the lower half of the medulla to the lower half of the dorsal region of the cord. For the most part the cavity occupied only a small area of the centre of the cord, but was surrounded by a relatively wide zone of gliosis, in which myelinated fibres were absent.

No abnormality was found at a higher level than the upper part of the pons, but the iter of Sylvius was T-shaped, with a ventral and two lateral prolongations. The ventral one extended between the oculo-motor nuclei, but did not reach as far as the posterior (median) longitudinal bundle. The lateral extensions almost reached the mesencephalic roots of the trigeminal nerves; they were curved slightly forwards, and their walls, which were everywhere covered with ependyma, were crenated and irregular, the ventral wall showing several small bays and creeks.

Beyond this nothing abnormal was found in the pons and mid-brain, except degeneration of ascending tracts, such as the mesial fillet on the left side, which had been interrupted by the morbid process lower down.

The highest section which showed any evidence of abnormal gliosis was one near the lower end of the calamus scriptorius, passing through the middle of the olivary body (fig. 4A). Here the fourth ventricle had a somewhat irregular contour, extending forward as a narrow slit between the hypoglossal nuclei as far as the dorsal margin of the posterior (median) longitudinal bundles. It also sent a shallower extension in on the right side between the hypoglossal nucleus and the dorsal nucleus of the vagus. Both these slits were lined with the normal ependyma of the ventricle. That in the middle line caused no distortion of fibres, but curving round the gliosis which covered the lateral slit a leash of myelinated fibres could be seen to which there was nothing corresponding on the left side.

At this level and extending downwards through the medulla for a short distance, there was a gross atrophy of the cells in the ventral portion of the right inferior olive, and, associated with this, a loss of the olivo-cerebellar fibres arising in them. An examination of sections at the highest level at which this lesion existed disclosed a small Y-shaped cavity. Its longest limb lay between the pyramidal tract and the olive; one of the shorter limbs passed ventralwards and mesialwards through the pyramidal tract, and the other dorsalwards between the olive and the mesial fillet (fig. 4B). From the walls of this cavity gliosis extended into the neighbouring tissues, chiefly along the hilus of the olive for about two-thirds of its extent, but also as continuations of the limbs of the cavity. In the more caudal sections through the olive no cavity could be seen, but the presence of gliosis was shown by the increase in the number and size of the glial cells, and to it the atrophy of the ventral part of the right olive appeared to be due. The lateral part of the pyramidal tract was smaller on the right side than on the left; the shrinkage of this tract was also probably due to its involvement in the gliosis.

Unfortunately serial sections were not made through the upper part of the medulla and the lower part of the pons, part of the tissue having become unusable owing to its long stay in Müller's fluid during the war, so that it was impossible to trace the extent of this cavity; but if either the cavity itself or a band of gliosis spreading out from it, had passed upwards for a short distance in the same relative position it would have interrupted the emerging fibres of the sixth nerve.

The most obvious loss of fibre tracts was in the mesial fillet on the left side, that is, in the more normal half of the medulla. This fillet had almost completely disappeared, and the place normally occupied by it had shrunken so that the inner border of the olivary nucleus came much nearer to the median raphe than on the right side. There was also considerable atrophy of the rubro-spinal tract on the right side—in fact, no bundle of fibres corresponding to it could be definitely made out. The descending root of the trigeminal nerve and the fasciculus solitarius were well represented on both sides, but on the right they were definitely smaller and paler than on the left. The descending root of the right vestibular nerve was represented by far fewer fibres than on the

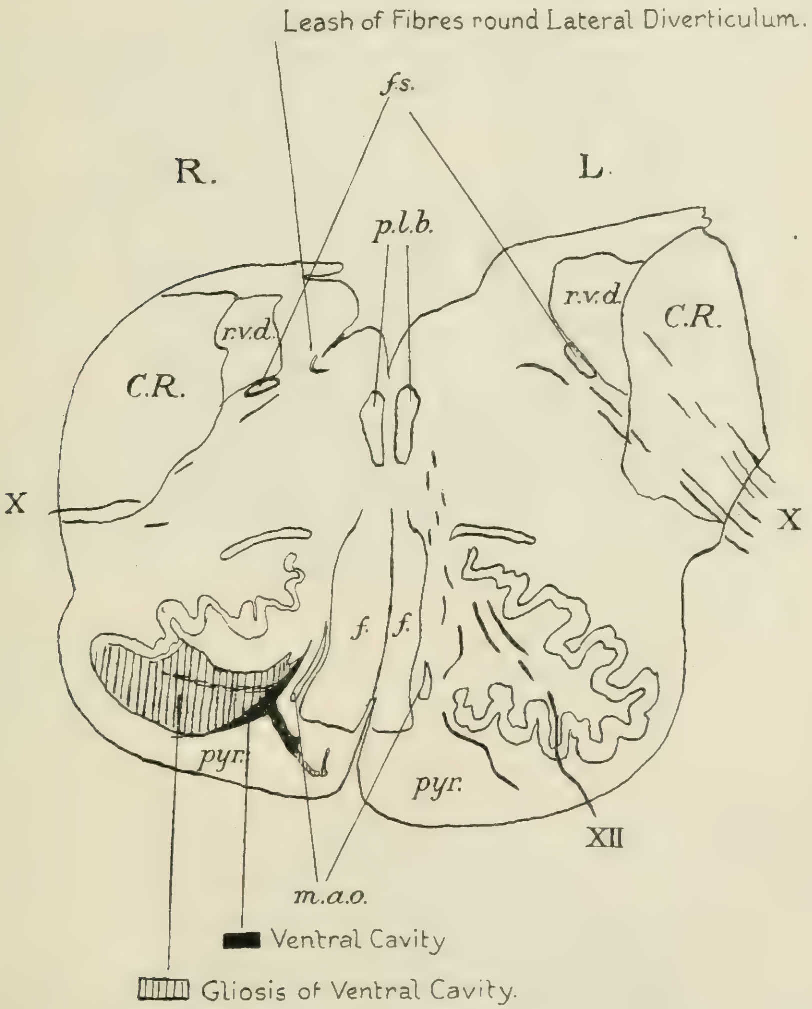


FIG. 4B.—*C.R.*, Corpus restiforme; *f.*, mesial fillet; *m.a.o.*, median accessory olive; *f.s.*, fasciculus solitarius; *p.l.b.*, posterior longitudinal bundle; *pyr.*, pyramid; *r.v.d.*, radix vestibularis descendens.

opposite side, and it and the right fasciculus solitarius had come to lie much nearer to the middle line than the corresponding tracts on the left side. In fact, the whole of the right dorso-lateral part of the medulla at this level had shrunk considerably. It appeared probable that the atrophy of these various fibre tracts was due to a retrograde degeneration of the fibres towards their cells of origin, owing to a lesion at a slightly lower level.

Some internal arcuate fibres were present on the right side at this level, but they were scantier than on the opposite side and more laterally placed. They were intermingled with fibres passing from the opposite olivary nucleus towards the restiform body.

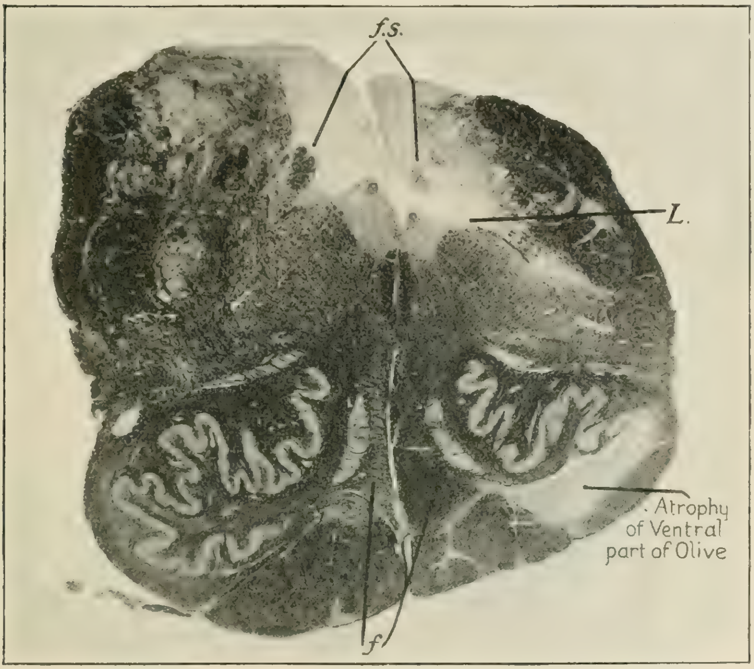
At a level of the medulla corresponding to the tip of the calamus scriptorius (fig. 5) the morbid process was evident as a line of gliosis which passed outwards on the right side through the dorsal part of the hypoglossal nucleus and through the substantia gelatinosa Rolandi (descending or spinal trigeminal nucleus) to about 2 mm. from the lateral surface of the medulla. This band of gliosis ran along the line of the large vessels, which pass dorso-mesially into the medulla between the olivary nucleus and the restiform body. At no level examined in this region was there any gross cavitation, but merely a broad line of gliosis which had interrupted the fibres and caused shrinkage of the parts through which it passed. Here also there was an extension of the cavity of the ventricle forwards between the two hypoglossal nuclei as far as the dorsal part of the posterior (median) longitudinal bundle, but no lateral extension, such as was seen at a rather higher level, could be made out. This mesial extension of the ventricular cavity had caused no obvious destruction of nerve cells or tracts.

The lateral line of gliosis had destroyed the dorsal part of the hypoglossal nucleus, the dorsal longitudinal bundle of Schütz, the major part of the fasciculus solitarius, the substantia gelatinosa Rolandi, and the rubro-spinal tract. It also appeared to have destroyed the descending root of the vestibular nerve on that side, as no fibres corresponding to it could be identified. The region of the nucleus gracilis was greatly shrunken and no fibres could be seen passing from it. Nor could any internal arcuate fibres be seen on that side, except a few laterally placed fibres which obviously arose from the olivary nucleus of the opposite side. As a consequence of this the mesial fillet on the left side was absent and the area it should have filled was shrunken to about half its normal breadth (fig. 5).

In spite of the atrophy of the fillet the posterior (median) longitudinal bundles lay opposite one another, in contra-distinction to what was seen in Case II (fig. 16). The pyramidal tracts, although rather paler than normal, did not show the gross atrophy seen in that case.

The ventral part of the right olivary nucleus was also degenerated here. This appeared to be due to an extension caudalwards of the gliosis surrounding the cavity which was seen at a higher level.

The cells of the right hypoglossal nucleus were atrophied and no root fibres could be seen passing from it. It seems probable that these fibres had been



Left. Right.

Fig. 5.—Medulla at the level of the tip of the calamus scriptorius. *f.s.*, Fasciculi solitarii; *f.*, mesial fillets; *L.*, lateral gliosis.

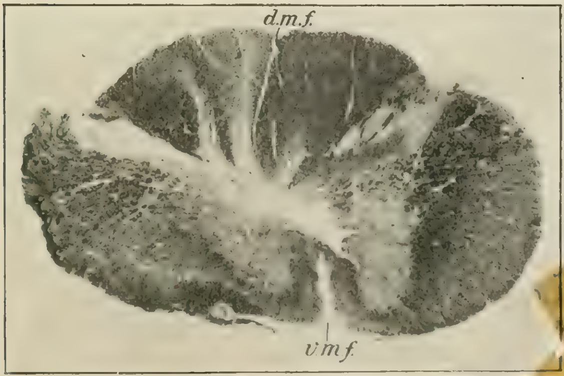


Fig. 6.—Cord at first cervical segment. *d.m.f.*, Dorsal median fissure *v.m.f.*, ventral median fissure.

interrupted by the gliosis and cavitation which lay between the fillet and the olive, and that their cells of origin had consequently undergone a retrograde degeneration.

Spinal Cord.—In the uppermost cervical sections (fig. 6), the central canal was represented by a solid cluster of ependymal cells. Areas of gliosis were present on the left side of it and behind it in the ventral part of the dorso-median septum. From the latter area a cavity extended along the dorso-mesial aspect of the right dorsal horn, the nerve cells in which were much less numerous than on the left side. From the ventro-mesial end of this cavity an area of gliosis ran a short way into the ventral part of the column of Burdach.

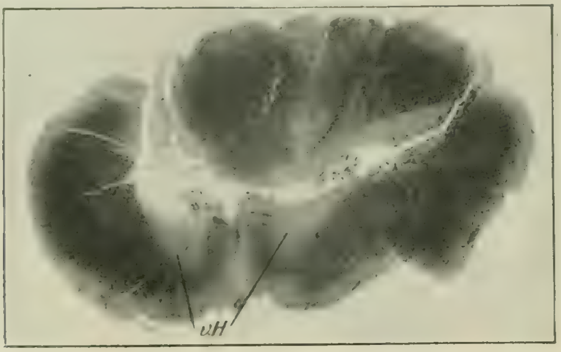


FIG. 7.--Third cervical segment of cord. *v.H.*, ventral horns.

At a rather lower level (fig. 7), the cavitation had extended through both dorsal horns and the grey commissure, occupying the situation of the central canal, of which no trace could be seen. At this level the walls of the cavity were lined with a definite layer of gliosis, which varied in thickness and, as in the higher sections, spread into the ventral parts of the column of Goll and the right column of Burdach. At the level of the seventh cervical segment the cavity had spread forward to reach the ventral median fissure, and laterally to the bases of both ventral horns. Extensions ran backwards a short distance down the left dorsal horn, and down the outside of the right dorsal horn almost to the margin of the cord. The wedges of gliosis which were seen at higher levels extending between the columns of Goll and into the right column of Burdach were still evident at this level, the lateral wedge being rather larger than it was above. Except for these wedges, the glial lining surrounded the cavity fairly regularly, and had a sharply marked outer border. The cavity itself was lined over a considerable part of its walls by a definite layer of fibrous tissue, which was continuous with the pia mater of the ventral median fissure. Many thick-walled blood-vessels lay, apparently free, within the cavity; the lumen of some of these was completely occluded, but in others red blood corpuscles could be seen.

The gliosis round the central cavity was, however, still more regular at the level of C 8 (fig. 8). Here it assumed a modified trefoil appearance and corresponded closely to the shape and extent of the central canal of the lumbar cord in Case II (fig. 22). It extended from the ventral median fissure laterally to the bases of both ventral horns, and dorsally a short distance down the dorsal median septum; the lateral areas of gliosis were club-shaped, and their outer ends swollen and rounded. Its outer border, that is the line at which myelinated fibres appeared, was everywhere clear cut and regular.

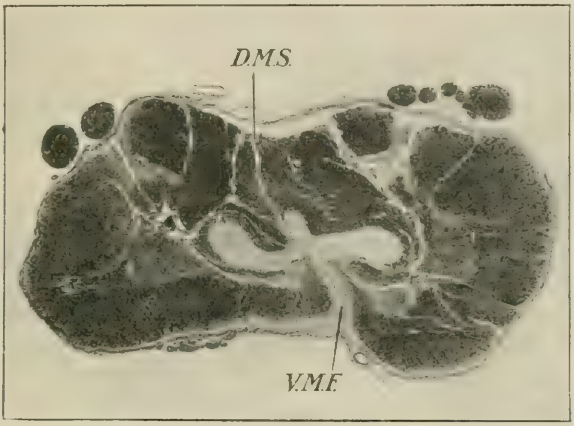


FIG. 8.—Cord at 8th cervical segment. *D.M.S.*, Dorsal median septum; *V.M.F.*, ventral median fissure.

Throughout the cervical region of the cord the nerve roots, both ventral and dorsal, were well myelinated and appeared to be of normal thickness. There was no gross atrophy of tracts apart from the areas of gliosis already described, but the left ventro-lateral column stained rather less deeply than the right.

In the upper thoracic region of the cord the gliosis was limited to an elongated oval running from the neighbourhood of the ventral median fissure through the region of the central canal and dorsally for about two-thirds of the length of the dorsal median septum. In the more caudal segments this area was separated from the ventral median fissure by some myelinated fibres of the white commissure, but its shape and extent remained otherwise constant. Its outer border was as definite and clear cut as in the lowest cervical segments. The cavity, which was limited to a small slit in its centre, showed no lining of connective tissue. The white matter of the cord appeared normal at this region, except for the extreme thinness of the white commissure, and for an area of pallor extending backwards from the dorsal end of the central gliosis along the dorsal median septum. In the lower thoracic region this central gliosis lay definitely behind the column of ependymal cells representing the central canal of the cord, and was separated from it by a few fine myelinated fibres, some of which ran longitudinally, while others passed across from one side of the cord to the other.

It is impossible from the material at our disposal to determine the level of the lower end of the gliosis in the cord, but it had ceased at the level of the first lumbar segment. From here downwards through the lumbo-sacral enlargement and conus medullaris the central canal was represented by a fairly large rounded clump of ependymal cells, which however did not show the circular arrangement seen in Case II. Their appearance was indeed similar to what is usually found in adult cords at this level.

Relationship of Clinical Signs to Pathological Changes.

In this case there are several clinical signs which it is very difficult to explain by the pathological changes discovered, although others admit of a simple explanation.

The anæsthesia over the area supplied by the right trigeminal nerve was accounted for by the involvement of the substantia gelatinosa Rolandi, and the degeneration in the descending trigeminal root on that side.

The wasting of the right half of the tongue was obviously a result of the atrophy of the nucleus and fibres of the right hypoglossal nerve. Both this and the paralysis of the right abducens nerve were probably due to the area of cavitation and gliosis which lay between the inner end of the right olive and the pyramidal tract. From the material at our disposal we are unable to give an anatomical explanation of the weakness of the muscles supplied by the fifth and seventh nerves on the right side. The nystagmus may be attributed to the lesion of the descending root of the right vestibular nerve.

This case presented the unusual feature that the anæsthesia on the right half of the body was nowhere dissociated. The area of complete loss of appreciation of light touch was exactly the same as that in which pin-prick and heat and cold were not recognized, and where one form of cutaneous sensibility was reduced but not abolished, the others were similiarly diminished. The apparent anomaly admits, however, of a simple explanation. It is generally believed that tactile impressions are conveyed to the thalamus by two sets of fibres; one set crosses in the cord along with the fibres conveying thermal and painful sensations to the opposite ventro-lateral column, while the other ascends in the dorsal columns to the dorsal nuclei of the medulla, and thence by internal arcuate fibres and the mesial fillet. But in this case the fibres passing from the right dorsal nuclei to the left fillet were interrupted by the gliosis which spread out from the floor of the fourth ventricle, and consequently this path, which in syringomyelia generally remains open for tactile impressions, was broken. No dissociation of cutaneous sensations coming from the right side of the body was therefore possible, since the only effective path for tactile sensibility was the same as that for thermal and painful impressions. The fibres of this path cross in the anterior commissure a considerable distance above their cells of origin in the dorsal horn, and are believed to retain their segmental arrangement until they have crossed. Therefore the fibres arising from cells in the right dorsal horn of the lower lumbar segments may have been interrupted in the lower thoracic region of the cord by a small lateral extension of the central disease, which, however, left intact the fibres arising at lower and higher levels.

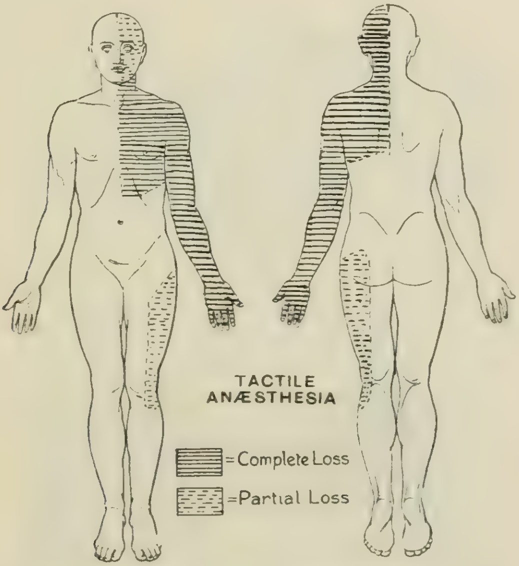


FIG. 9A.—Case II. Anæsthesia in 1902.

The second case which we are about to relate seems to be worthy of record because of the interesting character of the morbid condition from which the patient suffered, and of the long period over which it was possible to observe her and to note the progress of the malady.

She came (A. O.), a girl of 22, to see one of us (J. T.) in the out-patient room at Queen Square, in 1902, complaining of weakness in her left arm and hand which had been present for two or three years. This, she said, had com-

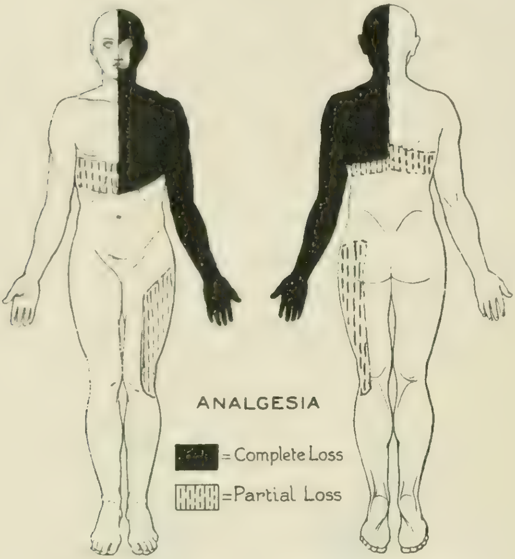


FIG. 9B.—Case II. Analgesia in 1902.

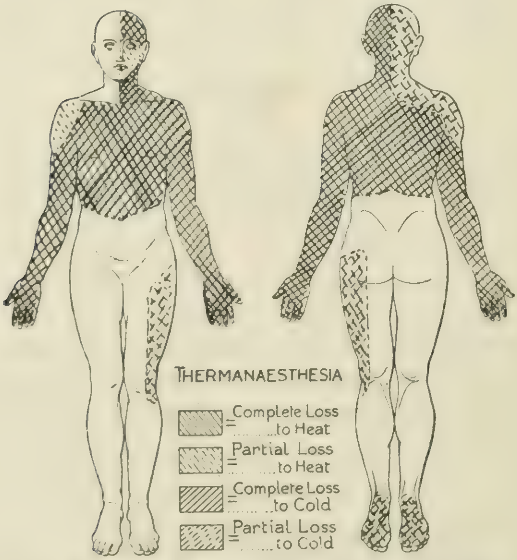


FIG. 9C.—Case II. Thermanæsthesia in 1902.

menced five years before, and was first noticed after she had had an abscess over the left first dorsal interosseous muscle. This abscess was opened without an anæsthetic, and the surgeon complimented her on her "pluck." But, as she laughingly observed, she deserved no credit, for the operation was absolutely painless! After this she began to have "pins and needles" in her left hand, which gradually spread up to her shoulder. Numbness was superadded, and in 1901 muscular weakness and contraction of the hand developed. She was admitted to the hospital in 1902. Apart from the weakness of the arm and hand and the anæsthesia shown in the charts (figs. 9 A, B, and C), nothing was noted except marked nystagmoid jerking of the eyeballs. She remained in hospital for two months, and was afterwards for a time at the convalescent home. There was no difficulty, even in the out-patient room, in making a diagnosis of syringomyelia, and examination in hospital confirmed the out-patient diagnosis. There was nothing significant in her personal history or family history, except that a sister had died of probably disseminated sclerosis.

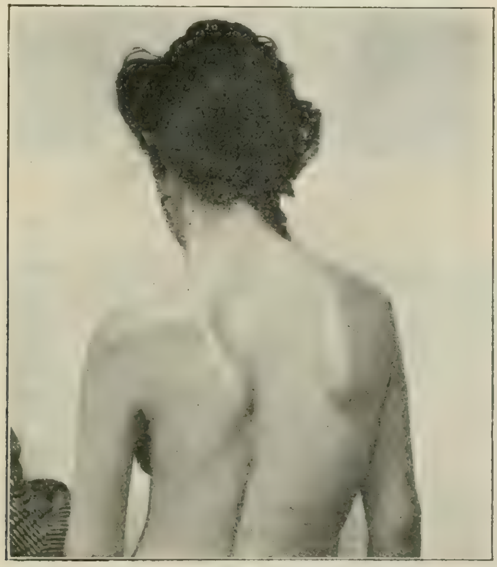


FIG. 10.—Case II. Showing scoliosis in 1905.

She was re-admitted to the hospital in 1905 and then she complained of weakness of the left leg as well as of the left arm. There was no wasting of the leg muscles, but there was an exaggerated knee-jerk on this side and also ankle-clonus. A definite lateral curvature of the spine had now developed (fig. 10). The left hand was a characteristic *main en griffe*, but the wasting was masked to a great extent by what has been described as a "succulent" appearance of the back of the hand and fingers (figs. 11 and 12); there was a purplish redness and an appearance as if the hand were cold, although to the touch it felt quite warm. The wasting had spread up the left arm to affect the muscles of the shoulder-girdle, and there was also some wasting of the muscles of the right shoulder. The nystagmus was more marked than before, but the sensory condition was little changed.

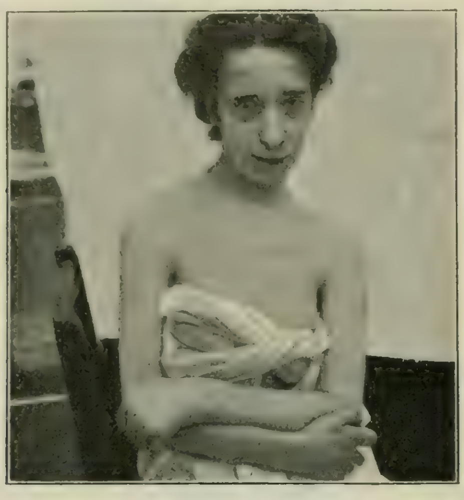


FIG. 11.—Case II. Patient in 1905.

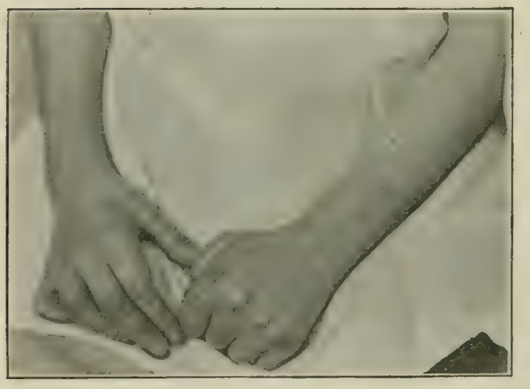


FIG. 12.—Case II. Showing swollen appearance of the left hand.

She was again admitted on May 15, 1909. The weakness in the left arm and leg had increased and there was wasting in the left calf. The plantar reflex was now extensor on both sides, and she complained of numbness of the whole of the left side. There was some unsteadiness in standing and a little difficulty in passing urine. The trophic change in the left hand was now

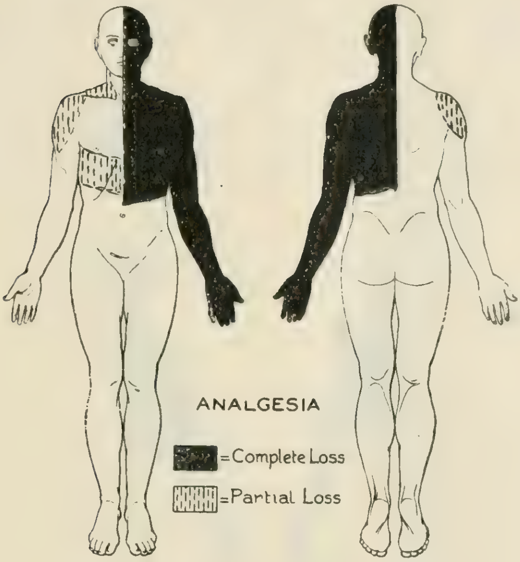


FIG. 13A.—Case II. Analgesia in 1909.

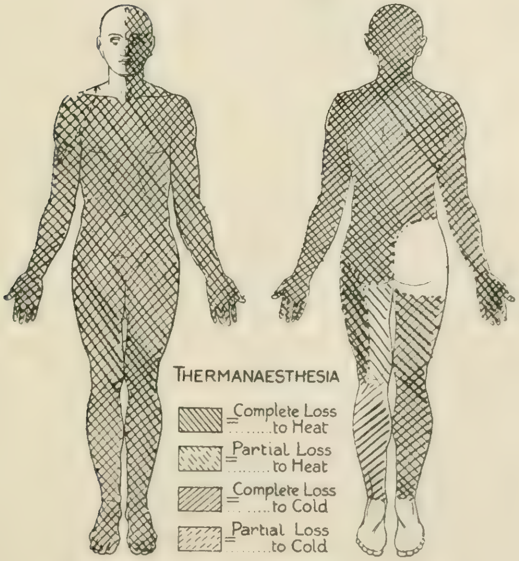

THERMANAESTHESIA
▧ =Complete Loss ....to Heat
▧ =Partial Loss ....to Heat
▨ =Complete Loss ....to Cold
▨ =Partial Loss ....to Cold

FIG. 13B.—Thermanæsthesia in 1909

more marked; the hand was swollen and of a purplish red colour all over. The sensory changes are shown in the diagram (figs. 13 A and B). She was again admitted on February 22, 1911. There was no marked change except that there was now slight wasting of the right hand, partial ptosis of the left eyelid, more marked nystagmus, and greater weakness of the lower extremities with increased spasticity of them. She had on this occasion a discharging painless boil on the right buttock; she also complained of some difficulty in articulating, although this was not noticeable. The analgesia recorded on this occasion is shown in fig. 14.

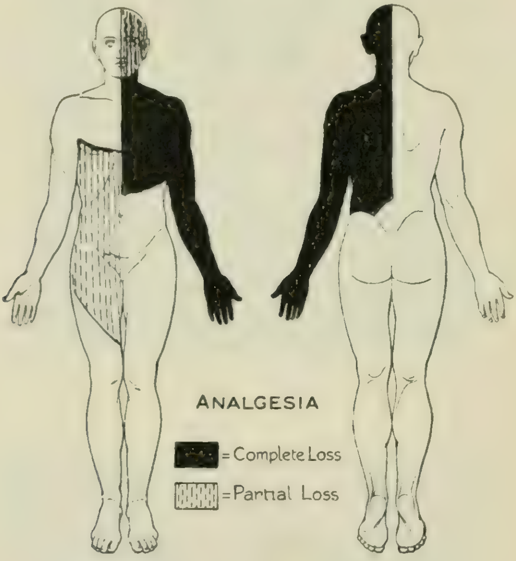


FIG. 14.—Case II. Analgesia in 1911.

She was in hospital also in 1916 but no change of consequence seems to have been noted. Her weakness in the upper limbs had increased and there was greater difficulty in walking. She was more pale and anæmic than before. There was no marked alteration in the condition of sensation.

On admission again, on March 3, 1919, her condition was one of great helplessness. She was quite unable to get about on account of the great weakness of the lower limbs, which she could only move a little in bed. Her left arm was powerless and her right almost as weak. She could not raise her head from the pillow. The nystagmus was marked and very coarse, and she complained that objects always seemed to be dancing up and down. The wasting was general but more marked on the left side; it included the sternomastoids and erectores spinæ. The knee-jerks and ankle-jerks were still active; there was bilateral ankle-clonus and each plantar reflex was extensor. The abdominal reflexes were absent, and there was some difficulty in passing

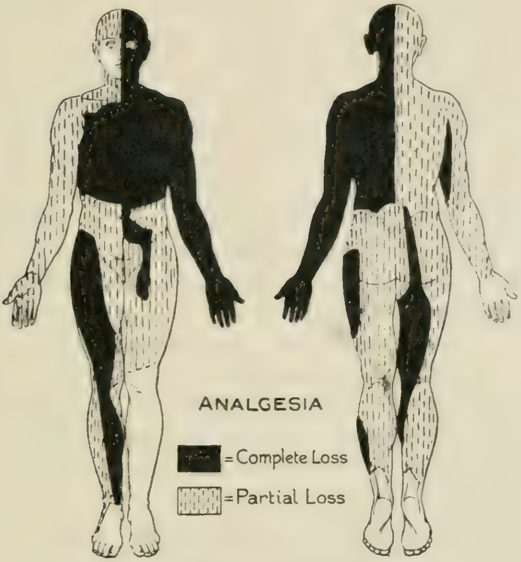


Fig. 15a.—Case II. Analgesia in 1919.

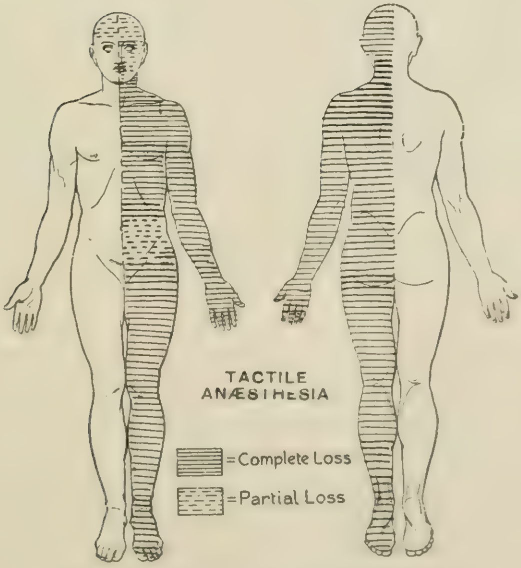


Fig. 15b.—Tactile anæsthesia in 1919.

urine. The sensory changes then present are represented in figs. 15 A and B. She was sent to the Convalescent Home at Finchley, where she died on April 13, 1921.

We have here, then, a case of a girl with nothing significant in her personal history, and the only point to note in the family was the possible occurrence of disseminated sclerosis in a sister. At the age of 17 she had a painless abscess on the left hand, the evacuation of which by incision was also unattended by pain. The subjective sensation of numbness in the left hand which was experienced a year later, in the course of four or five years spread up the left arm to the shoulder. At the age of 22, i.e., five years after the first symptoms appeared, she came under observation with wasting of the left arm and the disturbance of sensation depicted in the charts. From this time onwards there was a slow but steady extension of the numbness, wasting and weakness, with signs indicating involvement of the lateral columns and of the fifth cranial nerves. The muscular wasting and consequent weakness resulted in almost complete immobility of the limbs and trunk, and the sensory impairment also extended. Death occurred at the age of 42, twenty-five years after the commencement of the illness.

PATHOLOGICAL EXAMINATION.

A post-mortem examination was made on April 14, 1921.

The body was generally emaciated, but there was especially severe wasting of both upper limbs, perhaps rather greater on the right side than the left. There was a recent acute bed-sore over the back of the right shoulder.

The brain and cord were removed and suspended in 10 per cent. formalin saline.

The brain was abnormally long, measuring 19 cm. in length and 14 cm. in width. There was a slight degree of hydrocephalus, the anterior and posterior horns of the ventricles being about 2 cm. wide and having rounded tips. Apart from this the brain showed no gross abnormality above the level of the medulla.

The cord in the lower cervical and upper thoracic regions was a very thin-walled tube, filling the spinal canal and containing clear fluid like cerebrospinal fluid.

After fixation in formalin pieces from each of the segments of the cord were placed in Weigert's primary mordant, the cavity in them being filled with threads of pyroxylin. These dissolved out during the further processes of embedding in celloidin, leaving rings of spinal cord in much the shape that they would have assumed during life. Transverse sections from the mid-brain, pons, and medulla (the lower part of which was cut in serial sections), and from each of the spinal segments, were stained both by the Kultschitsky-Pal method, and by alum-hæmatoxylin with van Gieson's counterstain.

Pieces of the left ulnar nerve and a branch of the median (probably a sensory branch), and of the flexor sublimis digitorum and flexor carpi ulnaris muscles were also taken out and fixed in 10 per cent. formalin saline. The nerves were treated by the Weigert-Pal (Kultschitsky-Pal) and Marchi-Busch methods, and the muscles embedded in celloidin and sections stained with hæmatoxylin and van Gieson's counterstain.

The cavity.—The actual cavity extended from the middle of the medulla down to the upper border of the third lumbar segment. In the medulla it took the form of an irregular oblique slit which passed from the middle line of the floor of the fourth ventricle forwards and to the left towards the line of emergence of the ninth, tenth and eleventh left cranial nerves. In the upper cervical cord the slit extended through the grey matter of the dorsal horns and grey commissure, from the entrance of the posterior roots on one side to the corresponding point on the other side, being at some levels continuous with the central canal of the cord, at others separate from it. In the middle cervical region the cavity quickly widened and the cord from that level down to the lower end of the thoracic region was hollowed out into a tube; the width was greatest and the walls were thinnest in the cervical enlargement, and the tube gradually narrowed as it passed down through the thoracic region as far as the seventh thoracic segment; here it began to dilate again, but at the first lumbar segment it closed down abruptly to a small transverse slit which hardly extended laterally beyond the grey commissure. Below this for two segments there was a dilated central canal, but in the third lumbar segment it was occluded and there was no cavity in the remainder of the cord.

In every microscopic section in which cavitation was present there appeared also an area of gliosis; it was nearly always in contact with the cavity, at some levels surrounding it entirely and being widest about its angles, so that the conclusion was irresistible that the cavity was formed by the splitting of gliosed tissue and subsequent widening of the split by breaking down of its walls.

Occasionally small isolated areas of gliosis were found in the white matter, especially between dorsal columns (fig. 21), but on the whole it appeared that the gliosis-cavitation process overcame the grey matter with greater ease than the white; at many levels the grey matter was almost entirely eroded while a considerable amount of white remained, and, moreover, when the cavity came to the surface of the cord, as it often did, it generally did so along the lines of the posterior horns.

Changes in the medulla:—

Gliosis was carefully sought for in all parts of the central nervous system. No trace of it was found in the cerebral hemispheres, mid-brain, pons or upper medulla; its upper limit was in the medulla about the cerebral end of the hypoglossal nucleus, but this level was not accurately determined. At the level of the tip of the calamus scriptorius the morbid change was extensive and the oblique slit already mentioned was present (fig. 16). In the middle line there was an extension of the cavity of the ventricle between the hypoglossal nuclei. On the left side the slit passed almost to the periphery, following roughly the line of the tenth nerve roots, and not only was all the area behind it more or less degenerated, but it would appear from comparison with the right side that there had been considerable loss of tissue. The most dorsal part of the twelfth nucleus, the dorsal bundle of Schütz and the dorsal nucleus of the tenth and eleventh nerves, having lain in the line of the slit, were missing, and the descending nucleus of the trigeminus could not be distinguished. Dorsal to the slit the nuclei of the posterior columns were destroyed by gliosis, and the fasciculus solitarius showed degeneration and was devoid of surrounding cells. The area of the pyramidal tract was pale on both sides, especially on the right, some of its fibres having degenerated up to this level (retrograde degeneration). Emerging fibres of the hypoglossal nerve were fewer on the left than on the right, and though the nucleus of the nerve showed no gliosis it was deficient in cells.

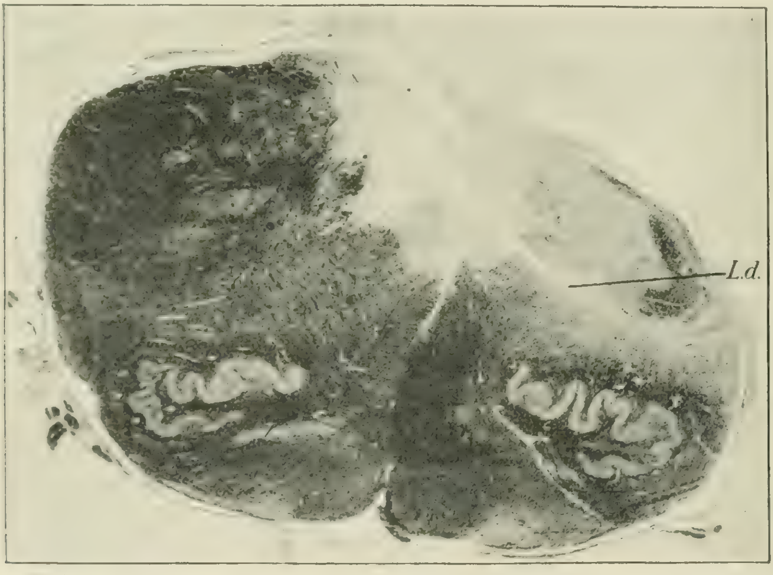
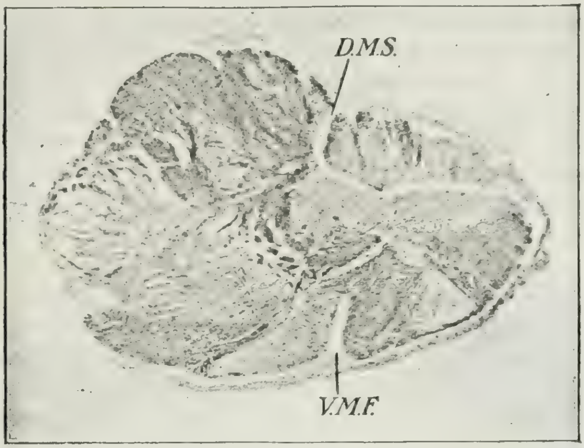


FIG. 16.—The right mesial fillet is severely degenerated, and the left fasciculus solitarius has almost disappeared. *L.d.*, Lateral diverticulum or slit.

In the lowest part of the medulla (fig. 17) the amount of gliosed tissue was much smaller relative to the cavity than at the level of the calamus, and at the decussation of the pyramids the loss of tissue on the left side of the medulla had been so great that this side was only about one-third the size of its fellow. The slit had inclined ventrally on attaining this level and had reached the periphery on the left, while in front of it a column of gliosis had formed round the central canal. By the erosion on the left side the left pyramidal tract had been completely destroyed just after it crossed, and by



Right. Left

FIG. 17.—The whole of the right pyramid and the lateral part of the left are degenerated. The internal arcuate fibres coming from the right dorsal column nuclei stain normally, but those from the left have disappeared. *D.M.S.*, dorsal median septum, *V.M.F.*, ventral median fissure.

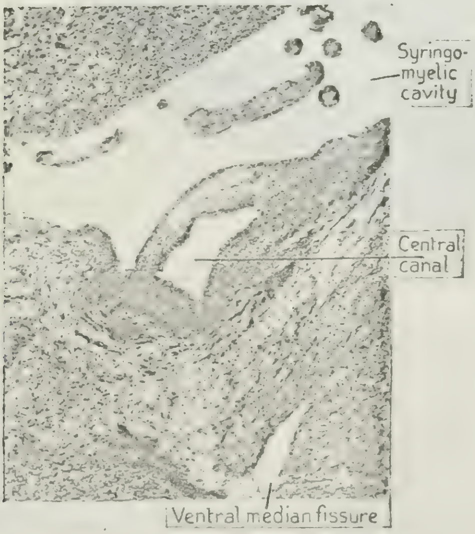


FIG. 18.—Case II. Cord at level of second cervical segment.

the gliosis round the central canal those fibres of the right pyramidal tract which had lain most posteriorly in the decussation were also interrupted. The interrupted fibres on both sides evidently degenerated both upwards and downwards from the lesion, with the result that immediately above its decussation the right pyramid was almost entirely degenerated and the left pyramid at the same level showed degeneration of its lateral part; the descending degeneration had an important influence on the appearance of the sections of the cord.

No central canal was present at this level but in its position there was an area of gliosed tissue with a large circular clump of ependymal cells. A little lower down, the canal itself appeared, with the ependymal cells quite regularly arranged around it (fig. 18).

These primary lesions gave rise to other changes of a secondary nature both at their own and at other levels. A consequence of the destruction of the nuclei of the posterior columns and of the interposition of the slit was the total absence of internal arcuate fibres in the left half of the medulla and therefore of the median fillet on the right: this default of the fillet on the right side was very striking in all sections up to the mid-brain. At the level of the calamus, the area from which the fillet had disappeared seemed to have shrunk, drawing forward the tecto-spinal and posterior longitudinal bundles (fig. 16).

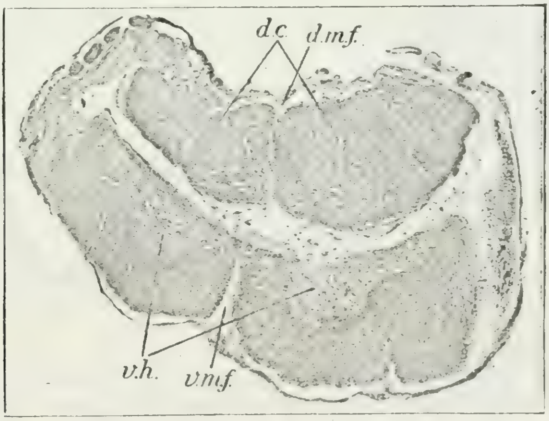


FIG. 19.—Case II. Cord at level of third cervical segment. *d.c.*, Dorsal columns; *d.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.m.f.*, ventral median fissure.

Another consequence of the interruption of the arcuate fibres was that the restiform body on the left side was much smaller than that on the right; in fact the left side of the medulla as a whole was smaller.

The ventral and probably the dorsal cerebellar tracts were degenerated both at this level and above. On the left side too, above the level of the disease, the rubro-spinal tract was degenerated (retrograde).

The spinal cord.—In the upper cervical sections (fig. 19) a wide fissure swept right across in an arc from the entrance of the posterior roots on the

left to the pyramidal tract on the right, reaching the periphery at both sides. Lying ventral to it in the middle line was the column of gliosis seen in the lower medulla, with the central canal now beginning to appear in it. Of the grey matter only the ventral horns and the tip of the right dorsal horn remained. The left pyramidal tract was represented only by a few fibres and the right pyramidal tract showed extensive degeneration; the dorsal columns of the left side were small, especially that of Burdach; on the right side the ventral part of the column of Goll showed considerable gliosis; the ventro-median columns of both sides and the ventro-lateral of the left had undergone partial secondary degeneration.

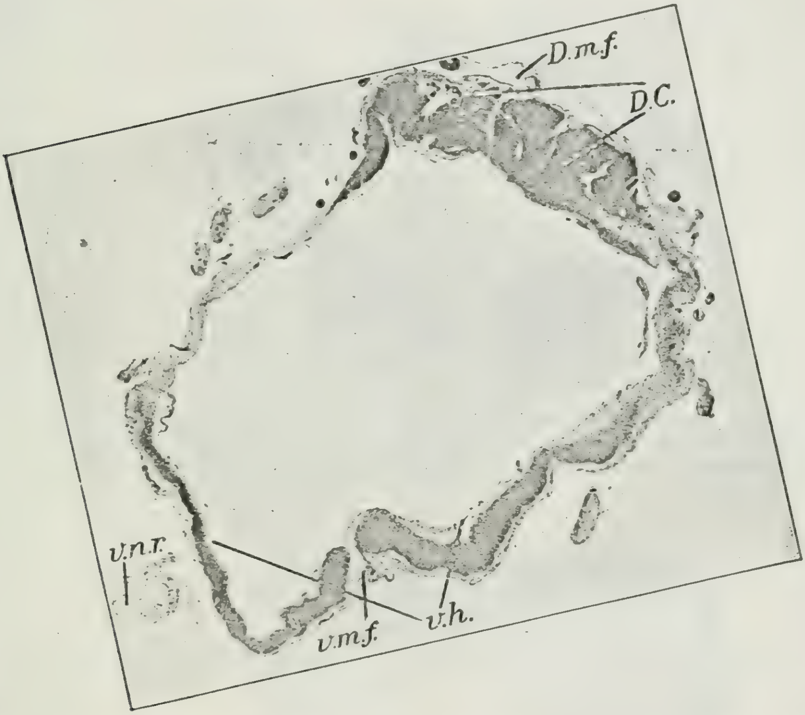


FIG. 20.—Case II. Cord at level of the cervical enlargement. *D.C.*, dorsal columns. *D.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.n.r.*, ventral roots; *v.m.f.*, ventral median fissure.

Passing downwards, the central canal first widened and then became continuous with the cavity. It was surrounded by a large number of cells, apparently ependymal, and the ependyma formed a lining for part of the ventral wall of the cavity. The cavity in the fourth cervical segment extended on both sides along the lines of the dorsal horns but did not quite reach the

periphery. At the edges of the cavity large numbers of cells were present but they did not form a boundary or lining; they were apparently glial.

In the cervical enlargement (fig. 20), the sections were irregular rings, the sides of which were formed chiefly by portions of the ventral and dorsal columns; the left pyramidal tract was completely degenerated and the right extensively but not completely so. Very small portions of the ventral horns were present.

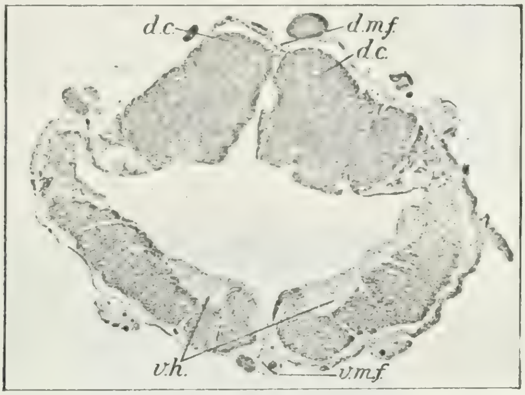


FIG. 21.—Case II. Cord in mid-thoracic region. *d.c.*, Dorsal columns; the pale oval area between them is a patch of gliosis extending from the central disease; *d.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.m.f.*, ventral median fissure.

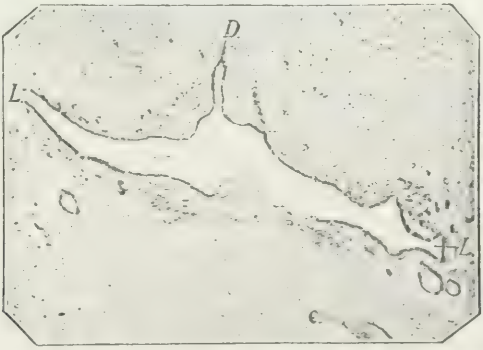


FIG. 22.—Case II. Dilated central canal at level of second lumbar segment. *D.*, Dorsal extension; *L.*, lateral extension.

Much the same may be said of the thoracic cord, but the ventral and dorsal columns were more compact, and the ring being smaller its walls were thicker. A greater part of the ventral horns persisted. More gliosed

tissue remained round the cavity, and at various levels the gliosis extended backwards between relatively healthy dorsal columns (fig. 21).

At the first lumbar segment the cavity, as has been said, narrowed quickly and appeared almost like a transversely dilated central canal. Its ependymal lining was not, however, complete, and it was surrounded by a zone of glial tissue containing a large number of cells which were ependymal in nature. The same appearances prevailed down to the third lumbar segment (fig. 22).

The outline of the cavity in the lumbar cord is particularly interesting, first, since it is similar to that of a stage of the developing canal, and secondly because a cavity of just this shape prolonged a little to one side, as it was in the first lumbar segment, would interrupt the crossing pain and temperature fibres from that side without affecting the touch fibres going to the dorsal column, and so produce a unilateral dissociated anæsthesia. A similar extension to the other side or a slight extension forwards would make the sensory loss symmetrical. One imagines that such a lesion if placed in the cervical cord might, in the absence of any interruption higher up, be the cause of the dissociated sensory loss in one arm, which was the first symptom.

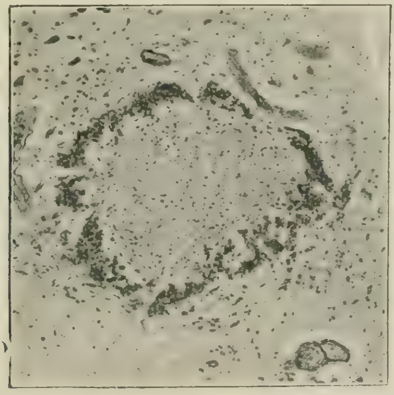


FIG. 23.—Case II. Section of fourth sacral segment ; ring of ependymal cells surrounding a pencil of glial tissue. Note the clear zones around the vessels.

The cavity was completely closed at the third lumbar segment. In the rest of the cord a slender pencil of finely reticular substance occupied the site of the central canal, containing irregular clumps of ependymal cells ; in the lowest segments these were arranged in a fairly regular ring around it (fig. 23).

Wherever gliosis or cavitation was seen, the large number and size of the vessels in and around the affected parts was noticeable; often they were actually free within the cavity. Apparently the vessels were more resistant to the process of gliosis and erosion than the nervous elements, with the result that those from the destroyed areas came together near the cavity.

The vessels which lay in or near an area of gliosis, but still surrounded by compact tissue, were usually encircled by a small pale-staining, translucent zone or by a small clear space; this appearance was best seen in the lower parts of the cord (fig. 23). This feature has been described by Schlesinger and by others.

Peripheral nerves.—Sections of the branch of the left median nerve showed no abnormality either by the Weigert-Pal or Marchi-Busch methods. The left ulnar nerve on the other hand showed gross degeneration. In sections stained by the Weigert-Pal method with van Gieson's counterstain, many of the nerve bundles showed no trace of myelinated fibres. In others there were small collections of fatty droplets which stained more deeply by the Weigert-Pal than the Marchi method; they appeared to be collections of altered myelin in the bodies of phagocytic cells and were evidence that some of the nerve degeneration had taken place at a comparatively recent date. Here and there were bundles of fibres which retained some myelin sheaths, but in most of these the proportion of fine to coarse myelin sheaths was very much greater than the normal. In some small bundles only a single myelinated fibre could be seen.

Muscles.—The flexor sublimis digitorum showed changes typical of a muscle which has degenerated in consequence of a lesion of its motor nerve. In cross sections some fibres appeared of nearly normal size, but their outline was rounded and in many the centre of the fibre stained palely. Other fibres were much smaller than normal; their shape was irregularly polygonal with rounded edges, and the nuclei of the sarcolemma sheath were increased in number and often had penetrated into the interior of the fibre. The muscle spindles and some of the nerve bundles in their neighbourhood (i.e., presumably sensory nerve fibres) appeared normal.

In longitudinal sections of this muscle it was possible to make out transverse striation in most of the fibres, but it was less well marked than normal, and in some of the fibres was almost invisible. Chains of nuclei running in or between the muscle fibres were very common, and most of the fibres showed an excessive number of nuclei within the sarcolemma sheath. In many places there were clusters of darkly staining nuclei lying between the muscle fibres.

In the flexor carpi ulnaris the changes were more varied, some bundles of fibres being comparatively healthy, others presenting an appearance similar to that seen in the flexor sublimis digitorum, and still others showing a later stage of the process of degeneration. In these the muscular tissue was represented by thin fibres with no sign of cross striation, containing chains of darkly staining nuclei which constituted the greater part of the substance of the muscle fibre. Transverse sections of this muscle showed in contiguous areas these three types of degeneration, and some bundles of partially degenerated fibres were surrounded by fibres which had degenerated completely.

Here, as in the flexor sublimis, the muscle spindles were healthy.

Relationship of Pathological Anatomy to Symptoms.

With such extensive destruction it is almost impossible to draw conclusions as to the causation of symptoms. A suggestion has been made already to explain the unilateral sensory loss by which the disease first manifested itself, but at the stage at which the patient died many pathological factors were at hand to account for her almost complete anæsthesia: as interruption of the spinal commissure throughout the cord, destruction of the dorsal root zone, lesions in the dorsal columns or their nuclei, and possibly destruction of the left spino-thalamic tract.

The weakness and wasting of the muscles of the neck and upper limbs, and the trophic disturbances in the latter, are explained by the extensive destruction of the ventral horns in the cervical and first thoracic segments. The spastic paralysis of the lower limbs was obviously due to the degeneration of the pyramidal tracts.

The dysarthria must be associated with the partial destruction of the left vagal and hypoglossal nuclei.

The complete sensory loss on the left side of the face and absence of the left corneal reflex may be referred to the lesion of the descending root of the left trigeminal nerve; that sensation was lost on both sides on the scalp and forehead considerably earlier than round the nose and mouth is explained by the fact that the descending fibres of the first division of the trigeminal nerve end at a lower level than those of the second and third divisions [11] [14]. It is stated that the fibres of the first division lie ventro-medial to those of the second and third divisions, and in sections just above the lesion the more ventrally placed fibres were pale, especially on the left side.

The smallness of the pupils and the partial ptosis of left upper eyelid are accounted for by destruction of the sympathetic centres in the cervical or upper thoracic cord.

The nystagmus is not so easy to explain. Liedler [7], from pathological and experimental evidence, concluded that nystagmus in syringobulbia is due either to a lesion of the descending vestibular nucleus of one side, or to interruption by the fissure of fibres passing from this nucleus to the posterior longitudinal bundle of the opposite side, and his view has been supported by Levy-Suhl [6]. In this case, however, no lesion of the descending vestibular nucleus was seen, and although a careful examination revealed no difference between the posterior longitudinal bundles, some of the fibres passing to them from the left vestibular nucleus must have been interrupted.

A comparison of these two cases from the pathological aspect reveals radical differences in some respects in spite of a close similarity in others.

The most striking contrast is in the relationship of the cavitation to the process of gliosis. In Case I there was much more gliosis than cavitation. For example, the lesion in the medulla appeared to be almost altogether due to gliosis, and very little cavity formation had taken place in that region. And in the cord also the amount of gliosis was everywhere much more extensive than the cavity, which, over almost the whole of its extent, was bounded by a thick wall of glial tissue. In Case II, on the other hand, the most prominent feature was the cavitation. In the medulla relatively little gliosis was seen, and, although lower down in the cord isolated areas of gliosis were present, they were small and insignificant in comparison to the size of the cavity.

This pathological difference may be correlated with the clinical histories : in Case I the morbid process ceased to progress about twenty years before the patient's death, for which it was scarcely responsible ; whereas in Case II it continued active, rendering the patient gradually more helpless.

With the scanty knowledge that we possess as to the nature of the pathological process at work in this disease, the relationship of cause and effect cannot be definitely stated ; but certain features presented by these two cases suggest a possible explanation of the arrest of the disease in the first case.

It has been noted that in Case II the ventricles were somewhat distended, the cervical cord swollen to considerably above its normal size, and the central canal in the lumbar region much dilated. In Case I, on the other hand, there was no evidence of hydrocephalus, but the iter of Sylvius was unusually large, and gave the appearance of having shrunk to the shape it presented in cross section during the process of fixation. Further, the thick concentric cuff of glial tissue which surrounded the cavity in the lower cervical and dorsal regions of the cord conveyed the impression that it had been formed in response to some tension or pressure from within the cavity. There is thus in both cases evidence that the cerebrospinal fluid in the ventricles and central canal of the cord was under abnormally high pressure, and that this was one of the factors leading to cavitation in the medulla and cord. In Case I either this pressure had fallen, or the glial tissue surrounding the cavity had become firm enough to withstand the destructive effects of the increased pressure.

It is usually taught, and is probably true, that the process of gliosis in syringomyelia is primary, and that it is the breaking down of the new-formed glial tissue which is responsible for the cavitation in the cord. But it must be remembered that glial tissue is in all probability endowed with a very slow rate of growth, and that although in the earlier stages of this process it is extremely fragile, in the later stages it is probably firmer than normal nervous tissue. Therefore, if the destructive process ceased for a time, the glial tissue might become firm enough to resist any further cavitation.

In Case I it is possible (and an examination of the cervical region of the cord bears out the suggestion) that the fluid had formed a channel by which it could escape into the subarachnoid space, and that the formation of this channel coincided with the arrest in the progress of the disease.

The association of syringomyelia with symptoms of increased intracranial pressure, such as headache and vomiting, has been observed by many authors. In some such cases the post-mortem examination has shown the existence of internal hydrocephalus. Such a case has been described by Grund [1]. This patient, the mother of four healthy children, commenced at the age of 24 to have headaches, which continued for nine years without the development of any other morbid symptoms. A year before her death they became worse, and were associated with giddiness and vomiting, and a little later weakness of the arms and paraplegic symptoms were added. Death occurred with Cheyne-Stokes respiration; indeed the whole symptomatology of the case suggested the diagnosis of intracranial tumour. The post-mortem examination, however, revealed no neoplasm, but hydrocephalus associated with syringomyelia and syringobulbia.

Hassin [2] has drawn attention to the increased pressure of the fluid within the cord in cases of syringomyelia. In such a case observed at operation the distended cord filled the theca, and no pulsation was seen in it. A slit made into the cord released clear fluid under great pressure and the pulsation in the cord was restored. In commenting on this case he makes the suggestion that the thickening so constantly found in the walls of the vessels in and around a syringomyelic cavity is a process of compensation for the increased pressure outside them.

The conception that increased intracranial pressure transmitted to the cerebrospinal fluid may be a dominant factor in the causation of syringomyelia is in some ways allied to the well-known theory of

Langhans [5]. He observed in four cases the association of syringomyelic cavities in the cord with tumours in the posterior cranial fossa, and considered that the latter by compressing the vertebral veins led to venous stasis and œdema in the cord, with consequent distension of the central canal and disintegration of the grey matter. This theory serves to explain not only cases such as those which Langhans studied, but also those in which cavities develop in the cord below the level at which it is compressed by a tumour.

And it is possible that a similar venous stasis may occur in the cases in which hydrocephalus is associated with syringomyelia, for the increased intracranial tension may push down the lower part of the cerebellum through the foramen magnum and thus compress the vertebral veins. A pressure cone of this kind was described by Grund [1] in the case he recorded, but it was probably a terminal phenomenon. It seems, however. unlikely that in the classical slowly progressive form of syringomyelia there is sufficient venous stasis within the cord to lead to cavitation. Nor is it common to find such cavitation in cases of cerebral tumour or hydrocephalus. Therefore, while it is possible that venous stasis may be one of the factors in the causation of syringomyelia it cannot be the chief or even an important one in the majority of cases.

Meningeal and arterial disease, by diminishing the blood supply to the central parts of the cord, may undoubtedly be the cause of cavitation in some cases. But in both our patients symptoms commenced before the age of twenty, and at the necropsy there was no evidence of meningeal thickening or arterial disease, except in relation to the cavities in the cord.

But there is evidence of another and probably more important ætiological factor in both of these cases, namely, a congenital instability of the glial tissue in the regions which the central canal of the cord occupies during fœtal life. In both cases the lesion in the dorso-lateral part of the medulla corresponded fairly closely to the lateral wing of the cavity which is formed during the primary flexure of the neural tube in this region. And in both cases there was also a ventral extension of the fourth ventricle similar to what is present before the fusion of the basal laminæ.

In the cervical cord in Case I the central gliosed area closely resembled the shape of the fœtal central canal, and lower down in the cord this area corresponded to its ventral and dorsal extensions. In Case II the central canal in the lumbar cord was an approximate reproduction of the fœtal canal, except that an ingrowth of glial tissue had replaced the ventral extension between the basal laminæ. Other considerations, such as the abnormal shape of the head, which was present in Case II and which has been described in other cases, emphasize the probability that the disease has a congenital origin.

It is difficult to explain the origin of the cavitation in the ventral part of the medulla in Case I on any of these theories. The clinical record suggested that this occurred at an early stage of the disease. In fact diplopia from weakness of the right sixth cranial nerve was the earliest symptom. Cavitation in this region is not common in syringobulbia, but has been recorded by Krauss [3], Raymond and Philippe [8], Rosenblath [10], Wilson [13], Grund [1], Spiller [12], and Rhein [9]. In the case described by Krauss the cavity lay, as in Case I, between the olive and the inner accessory olive, destroying the fibres of the hypoglossus. And in several of the other cases the cavity followed more or less exactly the line of this nerve.

An examination of the development of the hypoglossus reveals the fact that at an early stage of development the nucleus of the nerve lies relatively much nearer to the ventral surface of the medulla than it does at maturity. Several tract systems come later to lie ventral to it, notably the pyramid, the olivo-cerebellar system and the median fillet. The hypoglossal nucleus is thus shifted dorsalwards and its root fibres come to lie between the olive with its transversely crossing fibres to the cerebellum, and the two longitudinal tracts which constitute the pyramid and the median fillet. The arrangement of these tracts and the dorsal migration of the hypoglossal nucleus may make the line of its fibres a zone of lowered resistance, or of unstable cellular equilibrium, and so may lead to cavitation in the few cases in which this occurs.

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A STUDY OF THE CEREBRAL FIBRE SYSTEMS BY MEANS OF A NEW MODIFICATION OF ANATOMICAL METHODS. THE LATERAL WALL OF THE THALAMUS AND THE SAGITTAL PORTION OF ITS CEREBRAL FIBRE SYSTEM.

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THE amount of knowledge accumulated respecting the functions of the nervous system, in so far as those functions manifest themselves in movements on the part of the organism, is very large. A great number of most complicated phases of normal and abnormal behaviour have been correctly observed and are clearly understood. Yet our knowledge respecting the essential structures underlying such phases of behaviour remains small in amount and indefinite in quality. The diagrammatic and semi-diagrammatic representations of the arrangement of a great number of nerve conduction pathways, current even in the best publications on the subject, testify to the scantiness of a knowledge gained by distant and indirect methods of observation. As a matter of fact, a number of such diagrams rest upon pure hypotheses which, in their turn, have been deduced from certain kinds of behaviour.

Even our best method for the study of continuous pathways in the central nerve system, the so-called Marchi degeneration method, has its peculiar limitations. From the experimental application of this method man is rigidly excluded. Yet similar as is the basic plan of structure of the nervous system in all vertebrates, the human nervous system differs in many respects from the brain of even the highest anthropoid ape. In proportion to the size of the body the human brain is very much larger in bulk; and this increase in bulk implies both a vastly increased number of neurons, and a vastly increased complexity in their arrangement.

The study of the conduction pathways in the human brain by means of the Marchi method requires a rather involved combination of favourable circumstances. The lesion must be very small; the person must die within a period of some three weeks after the occurrence of the lesion, and there must be an opportunity for an autopsy. Such a combination of circumstances is sufficiently rare to make this excellent method of very limited application.

The opportunities for study offered by old lesions, in tissue stained by the Weigert method, are, of course, very much greater. Yet whatever stain is employed, the current methods of sectioning the tissue make its subsequent investigation a matter of extreme difficulty, and the results of such a study to a great extent uncertain. Except in a few situations the fibre tracts in the brain do not pursue any direction for more than a fraction of a millimetre. Owing to their sinuous course they are cut obliquely or irregularly no matter in which direction the section is made. What one sees in the best Weigert preparations of the brain is a beautifully variegated and almost hopeless picture constituted of millions of dots and streaks.

Careful dissection of properly hardened tissue, although the oldest, still remains one of the best methods at the disposal of the anatomist. In the dissection of the brain, however, one meets with certain dangers and difficulties. The chief danger is the fallacy into which one is almost certain to be led by habitual attempts to make microscopic deductions from macroscopic appearances. The greatest difficulty is that of retaining good records of the successive steps in the dissection. In the best photographs of such preparations most of the fine detail is utterly lost, while good drawings are rare, expensive and time-consuming. Yet unless many of the consecutive steps in the dissection of any one specimen are correctly recorded for subsequent study, criticism and comparison, the method, relatively crude as it is to begin with, must remain of correspondingly small value.

The modification of current anatomical methods to be described, obviates many of the difficulties and increases the certainty with which fibre tracts may be traced in the central nervous system. By means of current methods, the direction of lines and surfaces is inferred from the observation of points; by means of the modification to be described, points, lines and surfaces are directly observed. By the employment of this modification it has been possible to view a very large portion of an entire cerebral fibre system, such as the thalamic, pallio-pontine and others, each in a single section under the microscope; and to trace with comparative ease and exactness the course of bundles that have hitherto been represented only schematically.

METHOD AND GENERAL TECHNIQUE.

The method consists of two processes: (1) longitudinal sectioning and (2) serial dissections.

(1) Longitudinal sectioning is a method of preparing serial microscopic sections of any size in the plane of the course of a fibre-tract, or of an entire cerebral fibre system. The general technique will be given in this place, and the special steps to be taken in the preparation of sections of very large and complicated fibre systems will precede the description of each system.

The method may be employed in connection with a number of the ordinary stains and with either normal or pathological tissue.

(*a*) The particular fibre bundle or sheet is dissected out along the apparent course of its fibres. In well-fixed tissue such dissection is made comparatively easy by the use of the right kind of tools. In addition to the knife and scissors, the tools employed in the present work were small, spade-like, blunt-edged glass chisels, curved at an angle of about 100° at their ends. Such chisels are easily made in the Bunsen flame, and are very smooth and keep clean. Their curve enables one to get under the thinnest strand of fibres and to lift it out of its bed by leading the instrument along its under surface in the line of cleavage of the fibres. Such instruments, too, make it possible to reach fibre-strands in places which are inaccessible to a straight instrument without a serious distortion of the parts, such as the depth of the posterior and inferior extensions of the lateral ventricle.

(*b*) The detached strand is marked so that the relations which its several parts bore to the bed from which it was detached can be determined. A rough drawing accompanied by legends serves the purpose.

(*c*) The piece of tissue is placed on a numbered glass slide, the side in contact with the glass being carefully recorded. A pad of absorbent gauze, uniform or varying in thickness according as the tissue is of the same thickness throughout its extent or not, is placed upon the specimen, and is covered with a second glass slide of the same size as the first. This package is now tied with a strong string, the degree of pressure exerted in tying being such as to ensure the uniform application of the tissue to the glass slide on which it rests.

(*d*) If the Weigert-Pal stain is to be employed, the package is immersed in one of the mordanting solutions. There it remains for three or four days, or long enough for the tissue to retain its flat shape when the package is untied. It is then taken out of the solution, untied, and the top slide and the gauze pad removed. The strand of tissue is lightly fastened with a thread to the slide on which it rests and immersed once more in the mordanting solution, where it remains for the necessary length of time

If it is intended to use a stain which requires no preliminary mordanting of the tissue, the process of flattening it permanently may be accomplished by the use of alcohol or of any other fixative agent.

(*e*) When the mordanting is completed the glass slide with the piece of tissue tied to it is removed from the solution, washed, and treated with the alcohol and the ether solutions in the usual way employed in the preparation of Weigert-Pal celloidin sections.

(*f*) A glass slide is covered with tin (not lead) foil, and fastened to it by bending the edges of the metal around those of the glass. The tinfoil should be about 0·5 mm. in thickness. Such foil may be spread over the glass so that its surface is perfectly smooth and even. An attempt to use the ordinary very thin foil is almost certain to result in the failure of the subsequent procedures. The tin-covered slide is placed in a celloidin solution with the tin up. The slide bearing the tissue is removed from the alcohol-ether solution; the thread which holds the tissue to the glass is untied, and the tissue is gently pushed off the old slide and placed on the tin surface of the slide in the celloidin solution.

The vessel containing the celloidin solution should have a flat bottom, and it should rest upon a horizontal surface. The amount of solution in the vessel should be such that when it reaches the necessary final consistency its surface should rise above the embedded tissue for a height of about 3 or 4 mm.

(*g*) When impregnation and embedding is completed, a cut is made through the thickness of the celloidin, passing around the tin-covered slide. A convenient instrument is passed under the edge of the slide, it is lifted out, and its celloidin surface is fastened to a wooden block in the usual way. With the block resting on a table, the relations of the whole are then the following, from top to bottom: glass slide, tinfoil, tissue, a generous layer of celloidin, wooden block.

The edges of the tin are now bent away from those of the glass slide and the latter is removed. An edge of the tin is then held against the side of a pencil, which is rolled over the surface of the embedded tissue in such a manner that it becomes wrapped in the tinfoil. The metal is thus removed from the adjoining tissue, leaving behind a surface as straight and polished as a mirror.

The preparation is treated with alcohol or with cedar oil, in the usual way.

(*h*) The block is adjusted in the microtome in such a manner that the first cut will shave off a complete section. This is relatively easy since the tissue presents a perfectly even surface. In the present investigation it was found convenient to set the long diameter of the block as parallel as possible to the edge of the microtome knife; on the whole, therefore, the sections were in the same plane as, and more or less at right angles to, the apparent course of the fibres. The layer of celloidin between the tissue and the block permits the sectioning of the entire piece without waste. In this manner it was possible to produce longitudinal sections of strands of tissue 10 cm. long, 3 or 4 mm. in width and less than 1 mm. in thickness.

If the apparent course of the fibres in the tissue is not their true course, the fact is immediately discovered in the stained section. In a true tract the fine bundles of fibres may be followed in one and the same section in their entire length by merely moving the slide along the platform of the microscope. When a bundle leaves the main tract its deviation in a large field of uniformly parallel bundles is detected with the greatest ease. Moreover, in such sections perforating bundles are seen with a remarkable degree of definition, the cross-sectioned areas standing out prominently amid a field of longitudinal fibres. An example of such a perforating bundle is the auditory tract, which is cut across in the sagittal sections of the lateral portion of the thalamus. Those who have looked for this tract in normal Weigert-Pal preparations generally fail to identify it.

(2) In the microscopic preparations just described, the course of the fibre-tracts is observed in the two possible directions on a plane surface. Thus, in the illustrations which follow, the direction of the fibre-bundles is either up and down, or from before backward, or partly the one and partly the other direction. In order to leave as little as possible to the uncertain processes of deduction, the third direction was supplied by Serial Dissections.

For these dissections formaldehyde-hardened tissue was used. After through fixation the brains were removed from the formaldehyde solution, wrapped in towels and placed in loosely-covered jars. After two or three months the brain-tissue, but slightly shrunken, became sufficiently tough to permit the most detailed dissection.

A record of each step in the dissection is obtained by pouring on the preparation molten wax which, on cooling, furnishes a mould into which is poured plaster of Paris. When the plaster has set the wax is melted out. In this way a series of faultless reproductions of the several steps in the dissection of the hemisphere is obtained. The series may be as large as the investigator pleases. In the present study seventy-eight casts were made of as many steps in the dissection of one hemisphere ; fifty-seven of another ; only ten of a third ; and so on. For the study of the relations of the parts, and for comparison with the microscopic sections, such a series is invaluable. The moulding and the casting require but little time and skill. The wax never sticks to the damp brain-tissue, and projecting parts are pulled out of the mould with little difficulty.

SPECIAL TECHNIQUE FOR THE PREPARATION OF LONGITUDINAL MICROSCOPIC SECTIONS OF THE SAGITTAL PORTION OF THE THALAMIC RADIATION.

A curved instrument is entered between the corpus callosum and the cingulum, and the entire cingulum convolution, from the paraterminal body to the hippocampus, is removed. The association sheets between the cingulum and the other convolutions are next cleared away, until the callosal fibres are seen covering the entire mesial aspect of the hemisphere as far below and behind as the parieto-occipital and anterior calcarine fissures.

The septum lucidum is removed, the anterior pillar of the fornix cut as low down as possible, and the band of the fornix pulled away from around the thalamus. Below that band is torn off, together with the hippocampus and a part of the uncus, a short distance in front of the receding angle of the temporal ventricle. The association-sheets in the small sulci of the cuneus are cleared away. The floor of the anterior and posterior limbs of the calcarine fissure is cut through. The lateral ventricle is thus everywhere opened.

The superficial fibres on the dorsal and anterior surfaces of the callosal band—the fibres which face the antero-superior border of the hemisphere—are lifted up strand after strand and pulled off the mesial aspect of the hemisphere which they cover. This is continued until the thickness of the cut border of the corpus callosum is reduced to about one-half. At this stage it is found that the fibres of the callosal band, when pulled upon, break off easily at their point of contact with the hemisphere. These are the perforating fibres, and the fact that they have been reached is an indication that above the line of their entrance into the hemisphere the thalamic fan has been exposed on the mesial surface.

The ventricular ependyma is peeled off everywhere, except in the groove between the corpus callosum and the caudate nucleus and in that between the latter and the thalamus. In the former groove the ependyma is strongly adherent to the fasciculus subcallosus, a part of which may be torn away by an attempt to expose it; in the latter the ependyma is as strongly adherent to the stria terminalis.

In the posterior and inferior extensions of the ventricle the removal of the ependyma brings to view the fibres of the tapetum. This covering must be lifted with great care, especially in the inferior horn where it is very thin. Lateral to this layer, the entire expanse of the ventricle, except the narrow space around the thalamus which is occupied by the tail of the caudate nucleus, is carpeted by the fibres of the thalamic fan.

The instrument is now inserted into the substantia nigra and the thalamus separated from the fibres of the pes pedunculi. With the fan of the peduncular radiation as a lateral guide, the sagittally placed sheet of thalamic fibres is easily separated from the mesial aspect of the hemisphere in the frontal, parietal, and occipital regions. The expanded portion of the anterior commissure is a lateral guide in the separation of the thalamic sheet in the anterior half of the temporal ventricle. Lateral to the thalamic fibres in the posterior portion of the temporal and the lower half of the occipital ventricle is a layer of fibres converging towards the globus pallidus, and from this layer, too, the thalamic sheet is separable with ease.

The protruding mesial portion of the optic thalamus is now gradually torn away in the line of cleavage of the fibres, leaving a thickness of 5 or 6 mm. of its lateral wall.

The circumference of the large sheet thus obtained is serrated above, the serrations corresponding to the gyri and sulci at the superior border of the hemisphere. Below the circumference corresponds behind to the lower lip of the calcarine fissure; in front to the outer or lower portion of the hippocampal convolution. Still more anteriorly the gap in the outline of the circumference corresponds to the horizontal fissure, in front of which is the gyrus rectus.

The surface of the sheet which corresponds to the mesial aspect of the hemisphere is placed on a large slide, and the preparation treated as described under the heading of General Technique.

THE LATERAL WALL OF THE THALAMUS AND THE SAGITTAL PORTION OF ITS CEREBRAL FIBRE SYSTEM.

Fig. 1 was prepared practically from a single section. A few defects were corrected from four other sections. The size of these sections was nearly 13 by 9 cm. It is not possible to produce a single photomicrograph of an entire section of such size at a magnification at which the small bundles of fibres become visible. The alternative is to photograph or to draw the section in parts, and to put the fields thus reproduced together side by side in the proper order. For practical reasons the expedient of drawing was adopted. The Edinger epidiascope was used at a magnification of 25 diameters. The resulting huge drawing—1·8 by 2·3 metres—was then photographed and reduced to its present dimensions. The lines of the photograph were gone over with ink and the photograph bleached out.

The disadvantage of such an illustration is that although it gives a concrete idea of the general appearance of the stained section, the sharpness of its lines produces the impression of a diagram. Such an impression is true to the extent that each line in the drawing represents not a nerve-fibre, but a bundle of fibres in the section drawn. The advantages of such a drawing are the concreteness of the fairly correct idea of the appearance of the section which it furnishes, and the fact that it enables one to eliminate certain irrelevant features, such as the perforating bundles of the corpus callosum.

A number of photographs were taken from different parts of the sections employed in making the drawing, and some of these are reproduced in the illustrations. They serve the purpose of correcting the impression of the diagrammatic nature of the drawing. Such a correction is especially important in this case, since, as will be seen, the facts revealed in these longitudinal sections differ in several essential points from those of a number of investigators who based their conclusions on sections cut in the ordinary way.

In this study the Weigert-Pal stain has been used throughout. This stain furnishes no clue to the functional direction of a nerve-fibre. It is to be understood, therefore, that except where such a functional direction is explicitly stated, *it is nowhere implied in the forthcoming descriptions.*

The main bulk of the thalamic radiation has the general form of a fan open for about 300 degrees of a circle. The gap in the circle is the horizontal fissure. This fan is placed, on the whole, in a sagittal direction. A detailed account of its relations to adjoining structure will appear in a special paper.

The division of the thalamic radiation into several peduncles has no anatomical foundation. Dejerine [4] called attention to this fact, and other investigators agreed with him that the term "peduncles," in connection with the thalamic radiation, is to be used for convenience only.

Although it is true that the bundles of fibres of the thalamic fan are nowhere separated to the extent of justifying a division into peduncles, yet the several parts of the fan are each marked by certain characteristic features. These will be described as they appear when the thalamic radiation is viewed on a sagittal plane.

THE TEMPORAL THALAMIC RADIATION.

This does not include the auditory tract, which, in these sections, appears as a bundle of transversely cut fibres (fig. 1, IV).

The anterior portion of the temporal thalamic radiation has been described by Arnold [1], and has since been known as the temporo-thalamic fasciculus of that author. Since its fibres are spread out over the wide expanse of the wall of the temporal ventricle, however, this part of the radiation can hardly be called a fasciculus. In their course these fibres describe a series of curves which cannot be entirely explained by the curved lateral outline of the ventricular wall. From their junction with the postero-inferior portion of the thalamus, they proceed forward in the lateral wall of the temporal cavity. At varying distances from the receding anterior angle of the ventricle the fibres curve mesially within the floor, and the most anterior reach the mesial wall. All these turn backward, some within the floor, others within the mesial wall, and proceed in a posterior direction (fig. 1, I). The reason for this singular curvature of the fibres is probably to be found in the forward growth of the temporal lobe after the thalamic elements in it have been laid down, a probability which awaits corroboration at the hands of the embryologist.

In the long posterior part of their course the temporal fibres are arranged in parallel, rather coarse bundles, which are similar in appearance to those of the occipital radiation (fig. 1, II).

Before their junction with the optic thalamus, for a space of about 3 mm., the temporal fibres pass through the striate body, through the tail of the caudate nucleus. Within the substance of the latter they

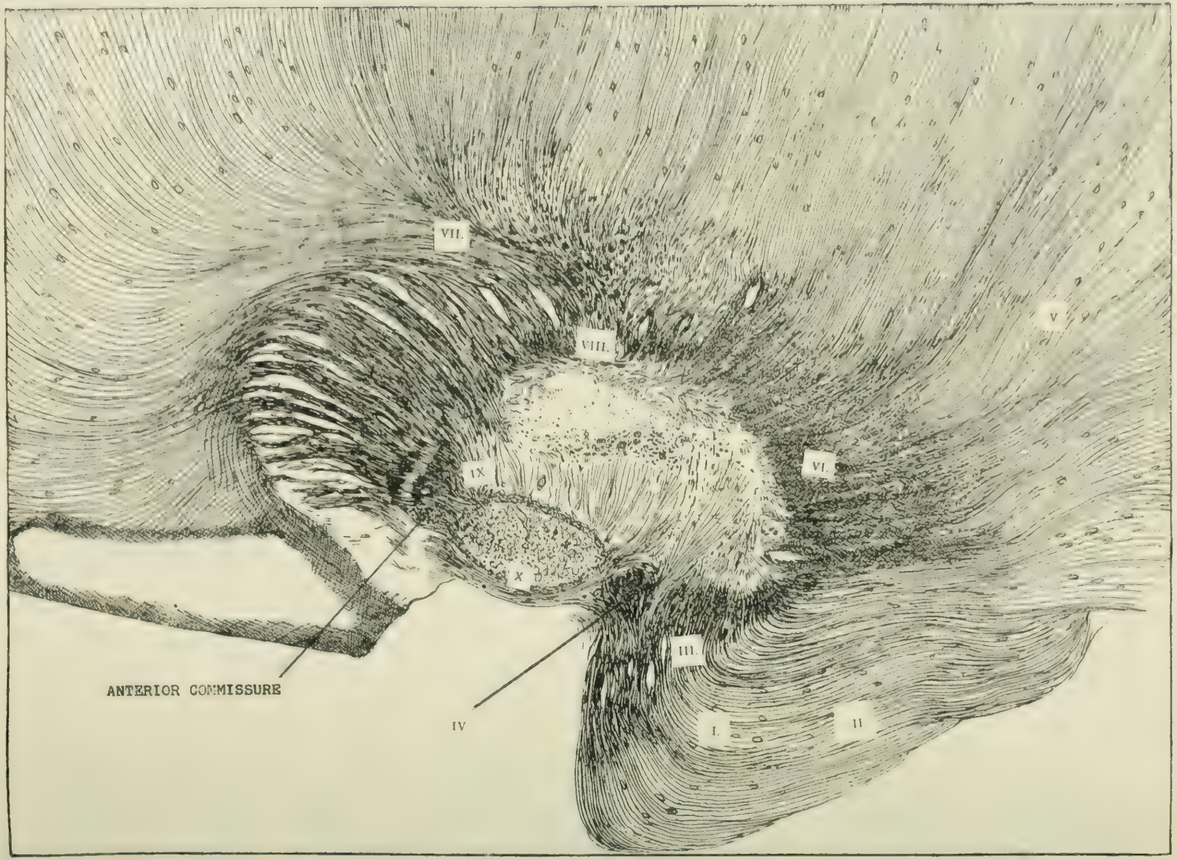

FIG. 1.—A drawing of the lateral wall of the thalamus and the sagittal portion of its cerebral fibre system. Details × 25.

are arranged in the form of flat bands, alternating with wide spaces occupied by the tissue of the striate body (fig. 1, III). The adjoining bundles show little tendency to interchange strands of fibres, as is the case in similar situations elsewhere, or to break up to any large extent into a brushwork of fibres similar to the brushwork to be described in connection with the occipital radiation. A number of fibre-bundles continue indeed distinct and parallel in an upward and backward direction until they have reached well into the outer middle portion of the nucleus of the pulvinar and the adjoining part of the lateral nucleus. That projection fibres from the temporal pallium stand (in the cat) in connection with the ventral region of the lateral nucleus, has been shown by E. Sachs [25] by means of experimental lesions. The nearly vertical course of the temporal fibres in the pulvinar gives that nucleus its characteristic streaked appearance.

Within the body of the thalamus most of the temporal fibres are situated immediately behind the auditory tract. This tract passes from side to side and is, therefore, cut across in these sections (fig. 1, IV). A smaller number of the temporal fibres, however, are placed in front of the auditory bundle, and are there intermingled with the fibres of a tract situated beneath the subthalamic body, which will be described later.

THE OCCIPITAL THALAMIC RADIATION.

Two characteristics distinguish this portion of the thalamic system· For the greater part of their length the bundles, neatly arranged and parallel (fig. 1, V, and fig. 2), are coarser in texture than the other fibre bundles of the thalamic system. At a distance of about 2 cm. from the posterior surface of the thalamus, they begin to break up into their constituent fibres, appearing at first like a row of stiff feathers, but gradually, as they approach the thalamus, assuming the form of a soft, matted brushwork, with the general direction of the filaments toward the thalamus (fig. 1, VI). In the study of the fibre systems in the longitudinal sections, this phenomenon will be encountered over and over again. It is always significant of the proximity of the fibre bundles to the nuclear mass in which they disappear. As this feature is rather conducive to hasty deductions respecting the beginning or the ending of a fibre tract, it is important to visualize it and to understand it.

If the handle of a camel's-hair brush be taken to represent a compact bundle, then the brush itself will represent the part of the bundle

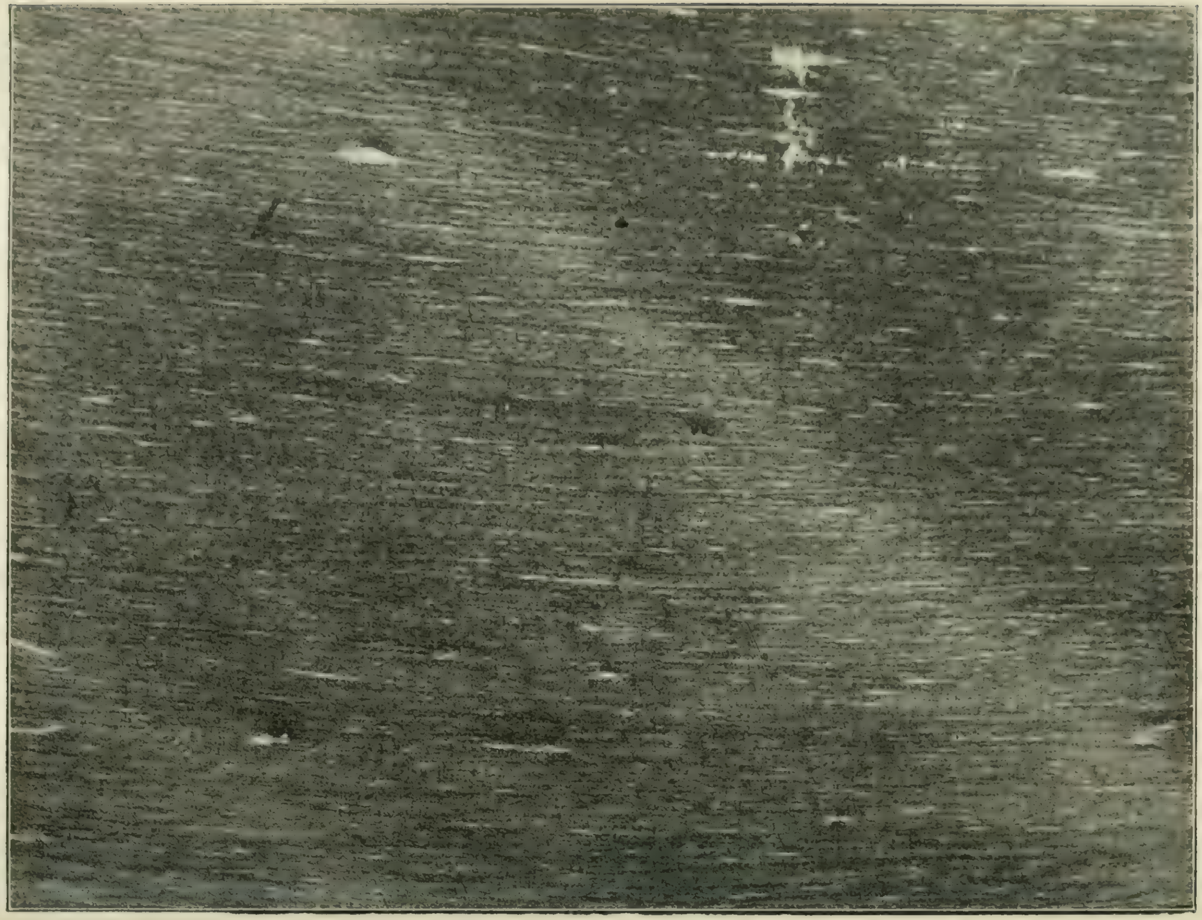

FIG. 2.—The occipital thalamic radiation. × 27.

where its fibres are spread more widely apart. If a number of such camel's-hair brushes, lying side by side, be embedded in paraffin or celloidin and then sectioned in the longitudinal plane, their appearance in each section will approximate that of the nerve bundles in fig. 1, VI.

In the neighbourhood of a nuclear mass in which a fibre tract begins or ends, its constituent fibres, gathered into compact bundles, must spread out. For this there are two reasons. One is that each cell is thicker than the fibre with which it stands in connection, and the entire nuclear mass, therefore, occupies a wider space than does the tract of fibres which it sends out or receives. The other is a rule which appears to hold good throughout the nervous system, central as well as peripheral, that there is a continual interchange of fibres between the adjoining bundles of a tract. That this arrangement holds good in the peripheral nerves, has been abundantly proved by the researches of Sherren [27], Heinemann [11], Langley and Hashimoto [13], McKinley [15], and a number of others. A careful inspection of the cerebral tracts shows that the finest parallel bundles which appear to retain a uniform thickness for a long part of their course, continually anastomose by means of very fine fibres, and that the whole tract is in reality a plexus of extreme intricacy. Owing to this it must be true that the mutual relations of the fibres in a nerve tract in the proximity of the nucleus in which it disappears are not the same as the mutual relations of the cells in the nucleus to which the fibres respectively belong. Thus of two fibres placed on the right of a nerve tract, one may pass to a cell on the right, the other to one on the left side of the nucleus. Hence the appearance of a matted brushwork of fibre bundles in the proximity of a nuclear mass to which they belong, seen in the longitudinal sections.

The phenomenon described, however, needs further investigation. It may be pointed out that in the neighbourhood of nuclei which are known to be efferent, such as the cranial and spinal motor nuclei, the emerging nerve-tracts are at first composed of parallel or converging fibres. In such nuclei each cell sends out but one nerve fibre, and these fibres then converge to form a nerve tract. There appears to be no reason for any matting of the fibres of an efferent bundle in the proximity of its nucleus, and none is observed. In the case of a tract near its nucleus of termination, however, the circumstances must be different. The fibres of that tract have changed places repeatedly, and in the neighbourhood of its nucleus each small bundle must break up into its constituent fibres, and the fibres must break up into thinner fibrillæ, in order that each may come into relation with a number of cells or cell processes in different parts of the nuclear mass. Such a tract might be expected, therefore, to have the appearance of a matted brushwork near the nucleus which it is to enter. It may be said that for the same reasons a tract containing both afferent and efferent fibres might be expected to present a mixed appearance near the nucleus in which some of its fibres originate and in which others end. Such a mixed appearance should be clearly observable in sections cut along the course of such a tract. In the sections examined in connection with the present study, however, nothing but a mere suggestion of this appearance has been observed, and on that no conclusion can be based. The only certainty so far reached is that in the neighbourhood of the nuclear aggregate in which the fibres of a cerebral tract gradually disappear from view, the bundles of that tract are always seen in Weigert-Pal sections to assume the form of a matted brushwork. When examining the course of the prefrontal part of the thalamic radiation an opportunity will be presented for contrasting sharply the appearance of its smooth fibre-bundles near and within the thalamus with the matted brushwork of the other contingents in similar situations.

On joining the nucleus of the pulvinar the rich brushwork of fibres into which the parallel and well-defined bundles of the occipital radiation have spread out, gradually breaks up and disappears.

The Parietal Thalamic Radiation.

In sagittal longitudinal sections of the thalamic radiation this part always appears defective. In contrast to the pictures presented by the other contingents, that of the parietal is marred by a number of thick, short streaks (fig. 1). A certain number of fibre bundles bend away from the sagittal plane in a direction which is at first forward, upward and lateral. In their forward course these bundles contribute to the formation of the fasciculus subcallosus which will be described later. They then proceed further laterally, in an upward and backward direction. Owing to their lateral inclination they are cut in short strips in these sections. Their appearance is distinct from the rest of the parietal bundles; they are very much thicker and converge below at an unusually large angle, between 45° and 90°.

The general backward sweep of the parietal radiation, as well as the number of laterally inclined thick bundles which it contains, demarcate it rather sharply in front from the frontal portion of the thalamic fibres. Behind, however, it merges gradually into the occipital radiation.

At a distance a little over 1 cm. from the optic thalamus, the fibres of the parietal radiation become aggregated into rounded bundles some 2 or 3 mm. in thickness. The spaces between these bundles are occupied by the substance of the striate body, through which they pass on their way to the thalamus. These bundles will be further considered in the next section.

THE FRONTAL THALAMIC RADIATION. THE FASCICULUS SUBCALLOSUS. THE STRIA TERMINALIS. THE FASCICULUS THALAMO-TEMPORALIS ARCUATUS.

In dissections of the body of the lateral ventricle, a bundle of fibres may be seen lying in the groove between the head and body of the caudate nucleus below and the corpus callosum above (fig. 3). This bundle is most prominent over the dorsal portion of the head of the caudate; it thins out over the body of that nucleus and disappears at the beginning of its tail. In certain specimens it attains a thickness of 3 mm. from above downwards at its thickest part.

The extent to which the current methods of sectioning the brain are conducive to error is well illustrated by the conclusions reached respecting the nature of the subcallosal bundle by universally recognized authorities. One conclusion is that it serves as a connection between the cerebral cortex and the caudate nucleus; another, that it is an association tract between different parts of the caudate nucleus; a third, that it is a fronto-occipital association tract.

H. Sachs [26] states: "The most important bundle which unites the corpus striatum with the grey cortex . . . is the fasciculus nuclei caudati. This bundle accompanies the caudate nucleus, running parallel with it . . . on the lateral wall of the lateral ventricle. . . . Lateral to this bundle is the corona radiata of the internal capsule. . . . Posteriorly it diminishes in proportion to the diminution in the thickness of the caudate. . . . from the bundle fibres pass into the caudate and become lost there. It appears that this bundle is composed of fibres coming from the frontal and the parietal parts of the cerebrum, and from the insula."

Koelliker [12] sums up his conclusions as follows: "This bundle accompanies the caudate nucleus lengthwise, throughout its entire extent, ventral to the corpus callosum, and forms part of the lateral

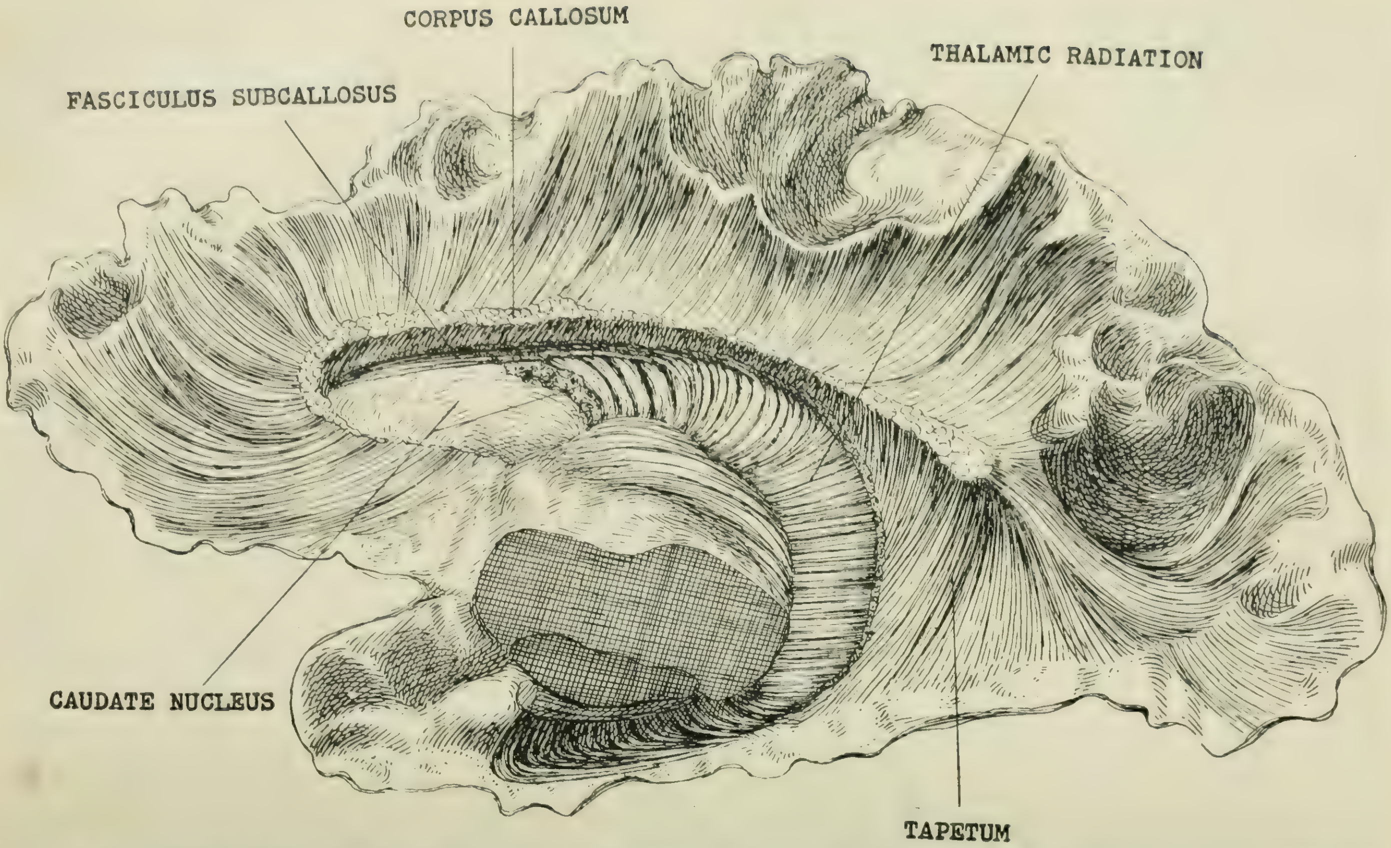

FIG. 3.—A drawing of a cast of a dissection on the mesial surface of the hemisphere. The body and tail of the caudate nucleus have been scraped away to expose the relations of the subcallosal bundle to the frontal and parietal bundles of the thalamus. A part of the tapetum has been cut away to show the course of the temporal and occipital thalamic bundles.

wall of the lateral ventricle. It diminishes in cross section from before backward. . . . Fibres enter the nucleus caudatus, where they become dispersed. . . . ”

Edinger [6] devotes considerable attention to this bundle. “In mammals,” he says, “there exists a small fibre tract which passes along the entire extent of the nucleus caudatus. It begins in front at the head of the ganglion as a few fibres which appear to come out of the head itself. This tract increases in size more and more posteriorly for a certain distance, then becomes smaller, in consequence of the slenderness of the tail of the nucleus. . . . The bundle lies in the angle between the nucleus caudatus and the roof of the ventricle; the fibres of the corpus callosum radiate over it. The fibres of this bundle appear to come from the nucleus itself and to return into it again. This is called the association bundle of the nucleus caudatus; but I cannot separate it sharply from the fronto-occipital association bundle which lies close to it.”

Bechterew [2] is very emphatic in his statement that this bundle consists of fibres connecting the cortex with the caudate nucleus. He states that degeneration of that bundle is observed principally after lesions of the frontal and parietal lobes, and to a less extent in those of the occipital lobe. After destruction of the frontal lobe it was possible to observe the degenerated area diminish from before backward, which, he thinks, points to the fact that the fibres originating in the frontal region of the cortex end in succession from before backward in the caudate nucleus. In a footnote the author cites Flechsig as being of the same opinion.

Probst [20], however, was not able to find any considerable degeneration in the subcallosal bundle in isolated lesions of the caudate nucleus. After destruction of the bundle in the anterior parietal region, the fibres degenerated in his experiments for a short distance only, and he could not follow their ends with certainty. He states, however, that more extended degeneration of the fasciculus followed deep destruction of the posterior cerebral region.

In the sagittal sections of the thalamic fan prepared by the method of longitudinal sectioning, the subcallosal bundle stands out with the greatest degree of clearness possible with the Weigert-Pal stain. With the unaided eye, as well as with all degrees of magnification, the bundles of fibres composing it can be traced from the frontal and partly from the parietal regions of the hemisphere, through the substance of the

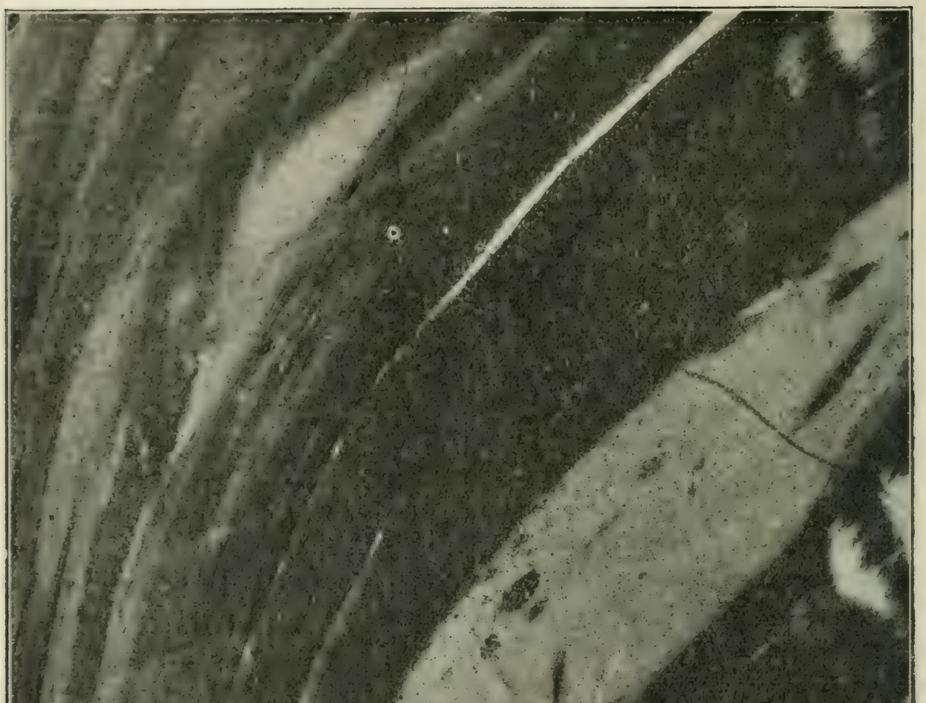

Fig. 4.—Fasciculus subcallosus. × 27. Above the direction of the bundles is almost horizontal. They are plainly seen to curve down, plunging through the substance of the caudate nucleus, on the way to the thalamus.

caudate nucleus, and into the optic thalamus. Fig. 1, VII, and fig. 3, indicate the course of the fibres composing the subcallosal fasciculus.

The fact is that the fibres between the frontal regions of the cortex and the thalamus pursue a rather intricate course. From in front and above they pass at first downward and backward in a series of graceful curves ; they then all turn backwards in an almost horizontal direction over the head and body of the caudate nucleus. In the horizontal part of its course the entire mass of fibres is packed into a single bundle of considerable width. At various distances from before backward this horizontal band gives off five or six fasciculi, which turn downward and plunge through the substance of the caudate nucleus to join the thalamus in the region of the stria terminalis.

A vertical or a horizontal section of the hemisphere passing through the caudate nucleus shows that no part of it is sufficiently separated from the rest of the corpus striatum to allow it to be regarded as a separate ganglion. To the anatomists who have described the subcallosal bundle the fact was well known that the existence of the caudate nucleus as a separate entity is a mere gross appearance. The form of that nucleus—a thick head in front, a body and a thin tail behind—is due mainly to the fact that from a mesial viewpoint the smaller thalamus leaves exposed a greater portion of the striate body above and in front than it does behind and below. Nor is the separation of the exposed from the concealed part of the striate body at all accomplished by the stream of fibres which perforate that body.

Even if it were true, then, that the fibres of the subcallosal fasciculus stand in connection with the cells of the caudate nucleus, it still remains difficult to understand why the fasciculus diminishes in thickness posteriorly, in proportion to the diminution in the thickness of the caudate nucleus.

A case of agenesis of the corpus callosum in the microcephalic brain of an idiot, described by Onufrowitch [19] and later by Forel [7], is responsible for a conception of the nature of the subcallosal fasciculus which still prevails. Notwithstanding the absence of the callosal band in this case, the tapetum was intact in the posterior extension of the lateral ventricle. Onufrowitch and Forel thought, moreover, that the tapetum was continuous in front with a bundle of fibres which passed between the cingulum and the caudate nucleus to the frontal portion of the hemisphere. They, therefore, concluded that the tapetum was not part of the corpus callosum, but that, together with the bundle of fibres which they saw pass to the frontal portion of the hemisphere, it constituted a fronto-occipital association tract. They called it the fronto-occipital fasciculus and identified it with the superior longitudinal or arcuate fasciculus described by Burdach.

Muratoff [18], in his experiments on dogs, found by the employment of the Marchi method that the amount of degeneration in the bundle described by Onufrowitch was relatively small when any single cortical area was injured. He also found traces of degeneration in it in lesions of the parietal cortex as well. He, therefore, disagreed with Onufrowitch that the bundle served to connect only the two areas implied by its name, and came to the conclusion that it was too complex in nature for any specific name and proposed to call it the fasciculus subcallosus. Respecting its identity with the superior longitudinal fasciculus of Burdach, he rightly pointed to the fact that the latter association tract is situated on the lateral side of the corona radiata, while the bundle in question is to be found on its mesial side.

Dejerine [4], using the same argument as did Muratoff, points out the error in identifying the subcallosal fasciculus with the superior longitudinal fasciculus of Burdach. He agrees with Onufrowitch and Forel that the subcallosal bundle is a fronto-occipital association tract. He brings, however, a number of facts to bear upon the nature of the tapetum, showing that it does contain a certain contingent of callosal fibres.

Wernicke [28] thought that the fasciculus in question was composed mainly of the fibres of the corpus callosum, but that it also contained a certain number of fibres from the frontal lobe. He declares, however, that he knows nothing further about its course.

That the subcallosal fasciculus is composed of fibres which extend into the large areas of the frontal and parietal cortex, has already been noted. When considering the course of the prefrontal and orbital fibres it will be seen that they curve for some distance upward around the head of the caudate nucleus, before plunging through its substance. In that situation, therefore, these fibres contribute to the formation of the anterior portion of the subcallosal bundle (fig. 1).

It can be easily understood that lesions of the occipital cortex would bring about degeneration of the fibres of the tapetum, if this is constituted either in whole or in part of callosal fibres. That lesions of the parietal and frontal regions of the cortex would result in degenerations in the subcallosal bundle is also easily understood. Yet that by no means implies the continuity of the frontal and parietal fibres with those of the tapetum. The difficulty lies in the obscure space which converges from behind forward between the posterior portion of the callosal band above and the optic thalamus below (see fig. 3). The greater portion of the lateral ventricular wall is there occupied by the tail of the caudate nucleus, above which the subcallosal bundle ends, while the fibres of the tapetum, which stream to or from the callosal band, curving around the tail of the caudate, overlap the ending of the subcallosal bundle. The suggestion of the continuity of the two is indeed strong. In any microscopical preparations where all the fibres are cut across and where all appear alike, it is quite impossible to recognize a line between the two. A lesion at this point would certainly involve both the fibres of the tapetum and those of the subcallosal band. Even some distance in advance of the ending of the bundle a lesion of the tract, by encroaching upon the closely adjoining fibres of the corpus callosum, might be followed by traces of degeneration in the tapetum on the one hand and in the frontal and parietal regions of the hemisphere on the other. In such a case, too, preparations containing vast numbers of fibres cut across must be misleading. In sections, however, where the thinnest bundles may be traced in their continuity, the posterior course of the subcallosal fasciculus is very plain (figs. 1, VII, and 4).

As to the nature of the tapetum, it is well to bear in mind that the last word has not yet been said on the composition of the corpus callosum. Hamilton [10] may have been wrong in his conclusions on its nature, but Beevor [3], who attempted to correct the error, was not altogether right. Cajal's silver impregnation sections are very convincing, and his [22] conclusion is that the corpus callosum is constituted in great part of collaterals of the projection and association fibres of each hemisphere. Roussy's [24] belief is "that a certain number of fibres depart from the optic thalamus and, by way of the corpus callosum, arrive at the cortex, and even in the thalamus of the opposite side." It is certain, too, that the corpus callosum contains a number of projection fibres of the ancient olfactory system. It must, therefore, be conceived as a commissural band which contains elements of many or even of all kinds of fibres of each hemisphere on their way to or from the opposite side. In the light of such a conception it will be readily understood how any portion of the corpus callosum may be present, though the rest be congenitally absent. If, therefore, any portion of the thalamic or the other fibre systems in the temporal and occipital regions attained a certain degree of development, the tapetum may very well have been present in the defective brain described by Onufrowitch and Forel.

The *Stria terminalis* or the *Stria cornea* is a prominent linear projection in the groove between the caudate nucleus and the optic thalamus. With certain differences in detail, it is the general agreement of Arnold [1], Meynert [16], Koelliker [12], Ganser [9], Edinger [6], Probst [21], Dejerine [4] and others, that in animals it is a fibre tract which begins in the masses of grey matter in the region of the anterior perforated space—the nucleus amygdalæ, the anterior portion of area pyriformis, the uncus, &c.—and which, after surrounding the optic thalamus, ends in the same masses again. Cajal [22] comments on the extreme difficulty of following this fibre band in man. His study of the tract in young mice has led him to the conclusion that the stria is both a commissural—by way of the anterior commissure—and a projection system of fibres belonging to the olfactory apparatus.

In his degeneration experiments on monkeys, dogs and cats, Probst [21] found the stria to degenerate in both directions. He could trace degeneration in front into the nucleus of Ganser, and behind into the tip of the temporal lobe.

By the method of longitudinal sectioning it has not been yet possible to establish the continuity of the fibre bundles composing the stria terminalis throughout their length in the human brain. The stria is most prominent over the superior (dorsal) part of the thalamus, in the groove between it and the caudate nucleus. In that particular situation the bundles of the frontal and parietal portions of the thalamic fan abut against the thalamus in a manner that might be very misleading in sections in which large numbers of fibres are cut across. At their junction with the thalamus the lateral portions of the stout frontal and parietal bundles pass down on the lateral surface of the lateral thalamic nucleus. There they at once break up into a matted brushwork which, in these sections, produces the very characteristic appearance of the lateral aspect of the lateral thalamic nucleus—the lamina medullaris externa. The mesial portions of the bundles in question, however, do not break up into a brushwork to the same extent. As they impinge upon the thalamus, they bend either forwards or backwards, and make a mesial bulge in the dorso-lateral groove of the thalamus, where they proceed for a considerable distance before sinking into its substance (fig. 1, VIII).

The effect produced by these frontal and parietal bundles as they impinge against the dorso-lateral edge of the thalamus is the same as when a row of camel's-hair brushes is pressed against a flat surface along its edge. Those hairs which strike the surface bend in different directions and the hairs of adjoining brushes will become intermingled; while those situated beyond the edge will pass straight down.

It is, of course, possible that mixed in among these thalamic fibres are others which pursue an arcuate course around the thalamus. It is certain, however, that the number of such fibres, if they exist in the human brain, must be very small. A number sufficiently large to form even a thin bundle could hardly fail to be detected in longitudinal sections of flattened-out tissue. It is also certain that the main bulk of the stria terminalis in man is produced not by such arcuate fibres, but by the linear bulge of the thalamic fibre-bundles as they impinge upon the lateral edge of the thalamus.

Much longer fibres than those which constitute the stria terminalis can be observed on the surface of the thalamus close to the stria. The thin superficial covering of fibres on the dorsal, posterior and inferior surfaces of the thalamus—the stratum zonale—may be peeled off with ease from the nuclear masses within. Ranson [23] has described such a long strand of tissue which he dissected away from around the thalamus, and which he called the *Fasciculus thalamo-temporalis arcuatus*. He gives, however, no account of the miscroscopical appearance of that strand, and its differentiation from the thalamo-temporal fasciculus described by Arnold is difficult. Serial microscopical sections cut in the longitudinal course of that band made in the present study show nowhere bundles of fibres extending from one end of the long strip to the other.

THE ORBITAL AND PREFRONTAL THALAMIC RADIATION.

The course of the fibres between the orbital and prefrontal regions of the cortex and the optic thalamus is quite unlike that of the other contingents of the thalamic radiation. From the prefrontal cortex the fibres at first curve downward and backward; from the orbital area they sweep upward and backward. Upon reaching the anterior border of the caudate nucleus, both sets of fibres curve abruptly upward, in front of and parallel to the outline of the nuclear mass for a distance of about 0·5 cm. In that situation the fibres contribute to the beginning of the subcallosal bundle. They are then gathered into thick strands which pursue a long downward and backward course through the substance of the anterior portion of the caudate nucleus, the lowest of them bending over the anterior commissure (fig. 1). In their course through the nuclear mass the bundles divide and anastomose at frequent and irregular intervals, so that this portion of the thalamic fan has the appearance of a coarse, crude network. It is important to understand, however, that this repeated division and anastomosis of the bundles takes place not only on a sagittal plane, but in a mesial direction as well. The consequence of this is that the mesially-bulging mass of the caudate nucleus above the anterior commissure is filled by these thalamic bundles. Since the fasciculi are bent in a mesial direction, a number of them are cut obliquely in sagittal sections where they branch out from their parent bundles, at the anterior and posterior borders of the head of the caudate nucleus.

Upon reaching the anterior end of the lateral portion of the thalamus, the thick bundles break up into thinner fasciculi which pursue a parallel course for some distance and then diverge. Throughout their long course these strands show no tendency to break up into a brushwork of fibres, such as is the case to a greater or less extent with the other contingents of the thalamic bundles.

It will be remembered that the anterior surface of the thalamus bears a rough resemblance to the narrower pole of an egg, in which the anterior nucleus is wedged in between the anterior portions of the converging lateral and mesial nuclei. Below, the anterior portion of the ventral nucleus is in contact with the lateral nucleus. The sagittal sections studied are those contained in the lateral portion of the thalamus for a thickness of about 5 mm. These sections, therefore, contain but a small portion of the anterior and of the ventral nucleus—their most lateral portions.

Lewandowsky's [14] researches tend to show that the anterior nucleus of the thalamus has no direct connection with the cortex. His conclusion is corroborated by the results of the present study to the extent that the thick bundles of fibres which are found in the anterior portion of the thalamus on its lateral side traverse this region without breaking up. This author is of the opinion, too, that there exists a pathway between the anterior nucleus of the thalamus and the subthalamic body. As will be presently seen, the work of other investigators in part contradicts this opinion. It has not been possible to establish in the present study whether such a pathway exists or does not exist. The longitudinal sections, however, do point to a possible source of error in this connection. As the bundles of fibres are traced in their longitudinal course downward and backward, a number of them are seen to impinge upon the capsule of the subthalamic body. Some of these bundles become intermingled with the dense network of the capsule and are thus lost to view; others, however, penetrate the capsule and traverse the substance of the subthalamic body for some distance. In the space between the anterior portion of the thalamus and the subthalamic body these bundles diverge; they are, therefore, more and more cut up in these sections, so that upon approaching the subthalamic body their continuation is indicated by a series of short strips (fig. 1, IX). In sagittal sections the subthalamic body appears filled with a multitude of islands of transversely cut bundles. In the midst of these, the short longitudinal strips of divided orbital and prefrontal bundles become lost. Their further course was not ascertained in the present study. Since this contingent of fibres arrives at the subthalamic body by way of the anterior portion of the thalamus, some of its most mesially lying strands might easily be mistaken for a pathway connecting the two structures.

Such a connecting pathway between the subthalamic body and the anterior nucleus of the thalamus, is to a certain extent negatived by the observations of Roussy [24]. After having destroyed the greater portion of the thalamus including the anterior nucleus in a monkey, he was unable to find any trace of degeneration in the subthalamic body.

This observation of Roussy's is incompatible with the picture presented by the sections in the present study. If bundles of continuous fibres traverse both the anterior portion of the thalamus and the subthalamic body, then their destruction between those points should be followed either by direct or at least by traces of retrograde degeneration in the subthalamic body. Yet in the experiment mentioned Roussy found the latter body to be intact.

That the thalamic radiation contains both corticofugal and thalamofugal fibres, has been abundantly demonstrated by the researches of v. Monakow [17], Bechterew [2], Dejerine and Long [5], Probst [20], Roussy [24], E. Sachs [25], Fukuda [8] and a large number of other investigators. If those prefrontal and orbital bundles which traverse the subthalamic body in the human brain contain cortico-fugal fibres, then an injury to those portions of the cortex should be marked by tracts of degeneration extending into the subthalamus.

v. Monakow [17] destroyed the greater portion of the cortex in a new-born dog (Gudden's method). Six months later an examination of the brain showed the thalamus very much reduced in size on the injured side, but the subthalamic body appeared normal.

After ablation of the posterior frontal region of the dog's cortex, Bechterew [2] found degeneration extending to the subthalamic body.

Of course, the posterior frontal region of the dog's cortex may not correspond to the prefrontal area of the human cerebrum. Yet even so, the findings in the present study are more strengthened by the positive results in Bechterew's experiment than they are weakened by the negative results in Monakow's case. The failure of development of a few strands of traversing fibres would probably cause too small a diminution in the size of the subthalamic body to be readily appreciated; while the observation of tracts of degeneration in that body after a cortical injury establishes the fact that cortical fibres either traverse or end in that body.

In the case where an old lesion involved all three frontal convolutions, Fukuda [8] found no atrophy in the subthalamic body. Whether this, too, should be discounted as a negative observation, or whether it signifies the fact that no fibres from the frontal portions of the cortex (as distinguished from the pre-frontal areas) pass into the subthalamic body, is for the present impossible to say. A concluding remark by the last mentioned author, in connection with two of his cases, throws some light on the subject. "It is not clear," he says, "where the bundles derived from the basal convolution-complex"—the prefrontal at the base, which include the orbital—"go . . . They certainly have no connection in the thalamus proper. At most they may pass to the most mesial portions, the tuber cinereum or the central grey matter of the third ventricle. . . ." This investigator, then, must have followed these bundles through the thalamus as far downward and backward as he could before he lost sight of their course.

My observations in the present study do not corroborate Roussy's [24] conclusion respecting the anterior thalamic nucleus as one of the sources of the anterior portion of thalamo-cortical fibres. Those lesions of the thalamus produced by this investigator, which involved the anterior nucleus, were large. They extended into the lateral portion of the thalamus and rather deep into its ventral and posterior portions. Fibres which may have their origin in regions behind and below the anterior nucleus would traverse it on the way to the anterior areas of the cortex. That large and numerous bundles do traverse the most lateral portion of the anterior nucleus, but which have their origin or their ending behind or below that nucleus is certain. If any of these fibres are thalamofugal, their destruction in their course through the anterior portion of the thalamus will be followed by their degeneration in a direction toward the cortex; and the impression produced may easily be in that case that the anterior nucleus is their source of origin.

After an experimental lesion in the anterior portion of the thalamus in a monkey, E. Sachs [25] observed degenerated fibres between the anterior thalamic nucleus and the external, lateral or capsular side of the caudate nucleus. In this case, too, a possible source of error must be pointed out. The orbital and prefrontal bundles traverse the antero-lateral parts of both the thalamus and the caudate nucleus. These bundles contain a contingent of thalamofugal fibres. In a lesion of the anterior part of the thalamus, a certain number of the latter fibres must, therefore, degenerate in their course through the lateral portion of the caudate nucleus. It will be remembered that while traversing the caudate nucleus, the bundles join and divide and join again in a multitude of ways. Points of degeneration would, therefore, appear as very much scattered in this intricate network, and difficult to follow beyond it.

TRACTUS SUBTHALAMICUS.

A well-defined band of very fine fibres appears in these sections immediately beneath the subthalamic body (fig. 1, X). It lies embedded therefore, in the substantia nigra, at its highest and most lateral portion. In front the fibres become dispersed and lost in the caudo-putamen, immediately beneath the anterior commissure. Posteriorly its fibres are intermingled with the temporal thalamic fibres in front of the transversely cut auditory tract. In a number of the more mesial sections the band appears to embrace and to merge with the auditory bundle. The nature of this band of fibres has not been ascertained.

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A NEW CONCEPTION OF THE ELEMENTS OF SENSATION.

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I.—Introduction.

We owe to Head our deliverance from the chaos which existed with regard to the afferent nervous system up to the time of the publication of his reconsideration of the distribution and function of the peripheral nerves. By means of investigations by measurable tests of each form of sensation, he was able clearly to demonstrate that what had been termed "diminished sensibility" was really a state in which some forms of sensation had been lost whilst others were retained. He was able to prove conclusively that "parts which have universally been considered to be areas of diminished sensibility turn out to be totally insensitive to certain higher forms of stimulation." In the study of the recovery of cutaneous sensation after suture of a peripheral nerve, he discovered two stages. During the earlier stage there was a gradual diminution in the area insensitive to pain produced by the prick of a pin, and to heat and cold, but the recovered sensibility was appreciably altered. The prick evoked a sensation which radiated widely and caused unnatural discomfort, and although the extremes of temperature could be appreciated no sensation of heat or cold was induced by intermediate thermal degrees. During the later or second stage of recovery the affected part began to become sensitive to light touch and to degrees of temperature which induced sensations of "warm" and "cool." With further improvement it became possible to discriminate two points applied simultaneously, and the characteristic radiation of the first stage gradually disappeared as more accurate cutaneous localization returned.

Such observations during recovery after suture of a peripheral nerve demonstrated the existence of two systems in cutaneous sensibility, which Head named the protopathic and epicritic, and it was thought that the former system regenerated more rapidly and with greater ease than the latter. The crucial test of this division into two systems was the classical experiment upon Head's own arm. In this experiment the radial nerve was divided at its origin from the musculo-spiral, and the musculo-cutaneous nerve at the point where it perforated the deep fascia, just proximal to its division into the two branches which supply respectively the anterior and posterior aspects of the pre-axial half of the forearm. Some days later it was discovered that, in addition to the larger area in which, except for the dissociation at the edges, there was a complete loss of cutaneous sensation, there existed a small triangular portion where normal sensation to light touches with cotton wool and Von Frey's hairs was retained, but there was insensitiveness to the prick of a pin. The dissociation of the sensation of this triangle was the reverse of that found at the periphery of the larger area, where the prick of a pin was appreciated but there was no appreciation of light touches with cotton wool. The prolonged investigations of these complementary areas of dissociated sensibility established the existence of the two systems in cutaneous sensibility, and proved that these two systems were independent and did not depend upon simply a modification of the same system of nerve fibres and end organs.

To these two systems found in cutaneous sensation Head added a third, deep sensibility, which was capable of responding to pressure, passive movement of joints, and pain caused by excessive pressure. He found that a part endowed with only this third form of sensibility possessed not only the ability to recognize a pressure stimulus, but also the power to localize it with remarkable accuracy. Furthermore it was decided that "the fibres subserving this form of sensation run mainly with the motor nerves, and are not destroyed by division of all the sensory nerves to the skin." Our knowledge of deep sensibility is based almost entirely upon an investigation of the residual sensation in the experiment upon Head's own arm. The nerves divided in this experiment were selected because it was thought that, since these nerves were usually considered as purely cutaneous in distribution, a large area of skin would be rendered completely insensitive and yet the sensibility of the subcutaneous tissues would be undisturbed. Observations will be advanced in this paper to show that it is anatomically impossible to isolate deep from cutaneous sensibility, and that, by employing methods which Head has used for the investigations of cutaneous sensation, it is possible to find after division of peripheral nerves at various levels most intricate types of dissociation in the various forms of sensibility grouped as "deep." Furthermore, having obtained an insight into the production of these dissociations, it is practicable during regeneration after suture to recognize two systems in deep sensibility.

My attention was directed to this subject during the progress of a study of the late results of secondary suture of certain peripheral nerves of the upper limb [7]—as the median and ulnar—since it became apparent that the sensory condition found did not conform with our present conception of the subject. The chief discrepancy had reference to deep sensibility, and most of the investigations recorded in this paper are concerned with this aspect of sensation. It was discovered in some patients, after suture of the median, that all the muscles—when tested individually—had recovered voluntary power and yet the hand was of slight practical service when the patient attempted purposive movements necessary on his return to work. These patients complained that they lost the grip of their tools, and on further inquiry it was found that they could use the hand fairly well as long as they concentrated upon the movements, but it failed to function satisfactorily as soon as they ceased to watch what it was doing. Several volunteered the information that the hand was useless in the dark or when they were unable to observe what they were trying to do with it. Such complaints were made by patients some three or more years after the performance of end to end suture, even when the cutaneous sensation had made a fair recovery and all the muscles, when tested individually, exhibited good voluntary power. It seemed clear that such a disability could only be due to a loss of afferent stimuli from joints, muscles, tendons and other deep structures. It was only practicable to investigate directly the extent of the recovery of fibres conveying sensory impressions from such deep structures as the joints. An investigation as to the sense of posture and the appreciation of passive movements in the finger and thumb articulations supplied by the nerve was carried out and it was discovered that these were generally lost, or at the best very defective, even when fully three years had elapsed since the time of the suture. This loss of appreciation, or defective recognition, of passive movement in the joints supplied by the nerves was found irrespective of the level of the suture; although, according to Head, there would be no serious loss of deep sensibility after section of the median or ulnar nerves low down, e.g., at the wrist. This inquiry into the recovery after end to end suture of afferent fibres from joints gradually directed me to the investigations recorded in this paper.

II.—THE ANATOMY OF DEEP SENSIBILITY.

By the subdivision of sensation into cutaneous (epicritic and protopathic) and deep, we are at once confronted with certain anatomical difficulties, which are emphasized in the hand and digits where much of the experimental work upon sensation has been performed. We cannot separate anatomically the fibres distributed to cutaneous and subcutaneous structures of any sensory nerve of sufficient size to warrant its use as a source of information about sensation. No nerve trunk or branch, of sufficient size to receive a name, has an exclusively cutaneous distribution. My own clinical investigations prove that the radial [8] besides supplying skin is distributed to certain articular structures, and careful dissection of nerves which have unfortunately been described as "purely cutaneous" will show that a large proportion of fibres terminate in the subcutaneous tissues. Of course such a gross method of investigation as dissection does not give us any information about the function of these fibres which can be traced into deeper structures, but in view of the clinical findings after division of the radial nerve (which is usually designated a purely cutaneous nerve), we must not assume that any nerve, of sufficient size to justify its selection for experimental work upon sensation, is purely cutaneous until it has been proved. In the course of this work the extreme difficulty of determining clinically whether the sensory fibres of a nerve are distributed solely to skin or not has become manifest, the chief hindrance arising from the fact that we cannot ascertain for certain whether some aspects of sensation are subserved by fibres terminating in skin, or subcutaneous tissues, or both. This difficulty is well illustrated by localization. From the experiments upon localization it is clear that fibres subserving this form of sensibility terminate cutaneously and subcutaneously. It seems possible from my own observations and those of others that discrimination may be also served by both cutaneous and subcutaneous systems;

but there are even greater technical difficulties to be overcome in making a decision with regard to this form of sensation. At first sight the experiment upon Head's own arm seems to establish discrimination as purely dependent upon a cutaneous supply, but it depends upon the *assumption* that the radial and the terminal branches of the musculo-cutaneous are purely cutaneous nerves, and since in a larger proportion I have found this not to be the case, the results cannot be accepted as proof that discrimination is only a cutaneous form of sensation. In the case of division of the median and ulnar it is clearly quite impossible to advance any proof with regard to this question owing to the complex anatomical distribution to subcutaneous tissues in this region. Whereas we know accurately the normal cutaneous distribution of the median and certain variations [6] in its cutaneous supply, we find that the corresponding deeper tissues receive sensory fibres from at least three sources. The subcutaneous structures of the palmar surface of the thumb, index and middle fingers are supplied from the median nerve direct by means of the digital branches, and from branches arising from the main trunk proximal to the wrist which probably run chiefly with the muscular branches, and so pass to their distribution along tendons. The subcutaneous tissues of the palm corresponding to the cutaneous distribution of the median are supplied, first by branches from the nerve itself as it breaks up in the palm, secondly by branches which pass down with the long tendons, and thirdly from the deep branch of the ulnar or perforating branches of the radial or both. The latter two possible sources of sensory fibres are shown by the fact that even after division of the median nerve in the upper arm, pressure and often pressure-pain can be recognized over the whole of the palm in some patients, and in all over a considerable part of the palm ; and similarly after division of both the median and the ulnar in the arm contact and pressure pain are appreciated over part of the palm, especially on the outer side.

The distribution to subcutaneous tissues in the case of the ulnar is not quite so complex, but sufficiently intricate to make it impracticable to isolate it from the cutaneous supply. In the hand deep sensibility is only in part subserved by fibres which run with muscular branches, since the digital nerves—which are generally regarded as cutaneous—definitely supply the articulations [8]. One form of sensation included under the term of deep sensibility is therefore invariably affected by division of the median or ulnar, whether the section of the nerve occurs at the wrist or in a more proximal part of the limb.

The complex anatomical arrangement of the sensory supply to the subcutaneous tissues of the hand makes it exceedingly difficult to investigate what has been termed deep sensibility; it is not accurate to regard it as the residual sensation after division of a purely cutaneous nerve unless we are certain that a nerve so designated has solely a sensory distribution to skin, and from the results recorded in this paper I maintain that we cannot so adjudge the radial nerve. Most anatomical text-books describe the radial as "purely" or "solely" cutaneous, but it seems evident that in the past anatomists have designated nerves as purely cutaneous on insufficient evidence. This appears to have misled Head and his co-workers into the belief that in "a human experiment in nerve division" only cutaneous sensation was destroyed, and deep sensibility persisted undisturbed.

From these conclusions it would appear that any division of sensation into cutaneous and deep must be regarded as artificial, and is apt to be misleading when applied to clinical work owing to the complex anatomical distribution of sensory fibres to the subcutaneous tissues.

III.—The Normal Anatomical Distribution of Afferent Nerves to the Interphalangeal and Metacarpo-phalangeal Joints.

After a few patients had been examined with reference to the extent of the recovery of sensory fibres supplying the articulations of the digits, a difficulty presented itself owing to our imperfect knowledge of the normal distribution of peripheral nerves to the interphalangeal and metacarpo-phalangeal joints. Consequently it became necessary to discover precisely the normal distribution of the various nerve trunks to the joints, in order to be able to estimate accurately the recovery which had occurred. The details of this part of the work have already been fully recorded in a recent paper [8] and it is necessary only to summarize the conclusions bearing upon deep sensibility.

In all fifty-one patients were examined and they were selected because it was known that a complete division of definite peripheral nerves of the upper extremity existed. Any patient manifesting such complications as division of tendons or limitation of mobility of joints was disregarded for obvious reasons.

The examination was first made on the normal side in order to make the patient quite familiar with the method and what was expected of him; secondly to provide a standard and control for comparison;

and thirdly to enable me to test the reliability and attention of the patient. It was surprising how few patients had to be discarded as unreliable when sufficient time was taken to make quite clear to them what was wanted, and enough patience was expended. A relatively large number, who were otherwise suitable, had to be omitted on account of arthritic adhesions. Each segment of the digit, above and below the joint to be examined, was grasped firmly by the lateral borders and then the joint was gradually and evenly flexed or extended. The segments of the digit must be grasped firmly, as Head [3] has pointed out, so that the additional pressure required to move the joint shall not be distinguishable and thus lead to the recognition of movement from impressions other than those arising from the articular structures. The movement of the joint must also be made as far as possible at a uniform rate and not too slowly. The patient was requested to state when he first felt any movement, and on answering was further asked at which joint it occurred, and also the apparent direction of the movement. The latter two questions were soon found to be of fundamental importance for any accurate investigation of the appreciation of passive movement in a *joint*, since it was discovered that patients were able frequently to recognize movement of a particular digit without possessing any knowledge of the joint at which it occurred or the direction in which it moved. Quite early in the investigation it became manifest that this recognition of mere movement of a finger was obviously dependent upon alteration in tension or position of the tendons (and consequent stimulation of the nerve endings in relation to them), and did not arise from any stimulation of afferent terminals in the bones, cartilage, and capsule of the joint. Several patients informed me that they felt the movement of something at the wrist and knew it was pulling on a finger, but were quite unable to discover from the sensation aroused at which joint the movement took place. Fortunately this source of fallacy was discovered at an early stage in the investigation, and errors arising from it were consequently prevented. From a review of other work on this aspect of sensation it seems possible that fallacies may have arisen in the past from this cause.

Another source of possible error, which was soon determined, arose from the difficulty patients had in expressing the joint at which the movement was experienced. Such a term as "first joint" was apt to be misleading, since some referred this to the metacarpo-phalangeal articulation, and others to the distal interphalangeal. Consequently it was found necessary at the outset of each examination to have a clear

TABLE I.—TO SHOW THE NORMAL VARIATION IN THE DISTRIBUTION OF AFFERENT NERVES TO THE INTERPHALANGEAL AND METACARPO-PHALANGEAL JOINTS.

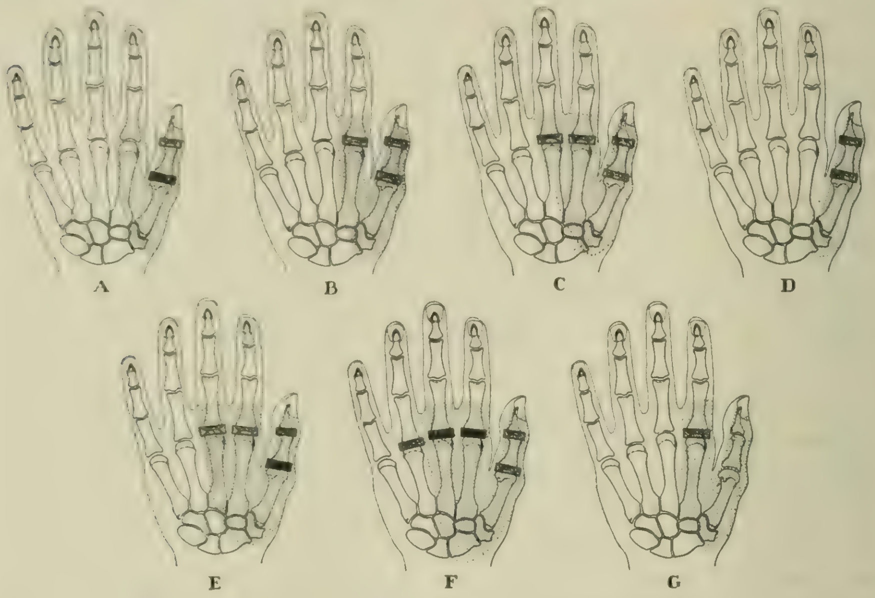
Thumb		Index			Medius			Ring			Little		
Interphal.	Met.-phal.	Distal interphal.	Prox. interphal.	Met.-phal.	Distal interphal.	Prox. interphal.	Met.-phal.	Distal interphal.	Prox. interphal.	Met.-phal.	Distal interphal.	Prox. interphal.	Met.-phal.
(1) Median chiefly Radial supplementary	(1) Radial chiefly Median supplementary	Median (invariably)	Median	(1) Median chiefly Radial supplementary	Median (invariably)	Median	(1) Median chiefly Radial supplementary	(1) Ulnar (Probably supplemented by median)	(1) Ulnar	(1) Ulnar	Ulnar (invariably)	Ulnar	Ulnar
(2) Median alone 42 per cent.	(2) Radial alone 15 per cent.			(2) Median alone 25 per cent.			(2) Median alone 42 per cent.	(2) Ulnar alone 25 per cent.	(2) Ulnar alone 25 per cent.	(2) Ulnar alone 5 per cent.			
	(3) Median alone 16 per cent.			(3) Radial alone 8 per cent.			(3) Radial alone 8 per cent.			(3) Very rarely branches from radial			
				(4) Very rarely some branches from ulnar			(4) Rarely some branches from ulnar						

understanding with the patient as to the terminology he adopted for the various joints. The results of this anatomical inquiry into the normal supply of the afferent fibres to the interphalangeal and metacarpophalangeal joints are summarized in Table I, but it must be understood that the percentages there stated can be regarded as only approximate, since only fifty-one patients were examined.

The most surprising result found in these examinations was that no difference in the extent of the loss of the recognition of posture and appreciation of passive movement was produced by section of the nerve under inquiry at different levels in the limb, a precisely similar distribution being found whether the nerve was severed in the upper arm, forearm, or at the wrist. In seven patients (median four, ulnar two, median and ulnar one), the division was at the wrist, and there had been no division of tendons, yet the loss of appreciation of passive movement was just as widespread and as profound as when the nerves had been divided in the upper part of the forearm. In twenty others the division had occurred in the forearm, and in a number of these in its distal part. The patients in the latter category did not manifest any loss of the recognition of pressure, yet the loss of appreciation of posture was just as extensive as after section in a more proximal part of the limb, even where one or more digits were completely anæsthetic to all forms of stimulation.

It is of particular importance to notice the condition found in fourteen patients in which the musculo-spiral had been severed, since the study of these patients really resolved itself into an investigation of the distribution of the radial and lower external cutaneous branches of this nerve to the joints. In two the recognition of passive movements appeared to be perfect in all the joints, but in the other twelve one or more articulations of the thumb or fingers were affected, and the extent of this distribution was found to be subject to considerable variation. It will be remembered that there was no disturbance of the perception of passive movement in Head's historical experiment upon which depends our present knowledge of deep sensibility; and it seems possible, from the fact that a similar result was found in only two patients out of fourteen, that this form of distribution is the exception rather than the rule. Furthermore in view of the evidence of the very frequent presence of sensory fibres in the radial for the supply of certain articulations of the digits, it is no longer possible to regard the radial as a purely cutaneous nerve.

In the course of this study a very intimate relationship between the variations in the cutaneous (epicritic) and articular distributions of the various nerves was observed, and this is illustrated in fig. 1 :—



■ = Complete loss of appreciation of passive movement.
▨ = Impaired recognition of passive movement.
░ = Extent of anæsthesia to lightest possible stimulations.

Type $A = 1$ patient.
,, $B = 4$ patients.
,, $C = 3$ patients.
,, $D = 1$ patient.

Type $E = 1$ patient.
,, $F = 1$ patient.
,, $G = 1$ patient.

FIG. 1.—To show the intimate relationship between the cutaneous (epicritic) and articular distributions of the radial nerve.

The loss of the appreciation of passive movement in the joints of the digits which exhibit no anæsthesia to tactile pressure is at first sight rather mystifying in view of our present conception of the pathway for the deep afferent impressions, i.e., along nerve-fibres which run chiefly with muscular branches and so reach the articulations by the way of such channels as tendons and blood-vessels. This view must largely disregard the digital branches of such nerves as the median and ulnar as a source of articular branches to the interphalangeal and metacarpo-phalangeal joints, and yet a simple dissection of these branches will demonstrate clearly fine filaments which pass to the periosteum of the phalanges and to the interphalangeal articulations. It may be presumed that these branches from the digital nerves are either afferent or vasomotor in function. The results found in the clinical examinations just recorded of patients suffering from division of the median or ulnar at the wrist, uncomplicated by any injury to the tendons, appear to show conclusively that some of these filaments are afferent in function and transmit information which enables us to appreciate the site, direction, and range of passive movement. Since the extent of the loss of appreciation of passive movement was not altered by the anatomical level of the section of the nerve, it appears that few, if any, fibres subserving this form of deep sensibility run with the branches to forearm muscles, the tendons of which are inserted into the phalanges. Several patients suffering from division of the median or ulnar at the wrist were able to recognize "movement" of a particular finger, probably as a result of alteration of tension or position of the long tendons; but it was clear that this knowledge was not produced by stimulation of afferent terminals in the neighbourhood of the joint, since some of them explained that they felt "the pull at the wrist," and so "guessed a finger was being moved." None of these were able to recognize at which joint the movement occurred, or in what direction it was made.

These conclusions have been verified upon a number of patients examined three or more years after suture of the median or ulnar nerve at the wrist, who at the best still exhibited very defective recovery of the appreciation of passive movement in the joints supplied by the affected nerve. From these investigations it appears that the digital nerves are the only important source to the joints of branches which transmit impulses that enable us to recognize position and movement.

On applying this knowledge to the examination of large numbers of patients upon whom end to end suture of the median, ulnar, or musculo-spiral nerves had been performed, it was found that this form of sensation, irrespective of the level of the suture, failed to show any signs of recovery until a very late stage—a time when there was evidence of return of epicritic sensibility.

IV.—LOCALIZATION.

The findings with regard to spacial recognition in three dimensions led me to investigate other aspects of deep sensibility.

At present it is believed that pressure is localized with remarkable accuracy even when there is a complete loss of cutaneous sensibility, and it is surmised that this form of sensation is dependent upon afferent fibres which run in muscular, articular, and subcutaneous branches.

Hitherto, no perfectly satisfactory method for testing accurately tactile localization has been evolved. Most methods now in use only demonstrate very gross defects, and fail to furnish measurable results. The tests most frequently adopted in the investigation of tactile localization only show such a gross error as failure to recognize correctly the segment of the digit upon which the pressure has been applied—a defect which I have found to occur several times in apparently normal individuals [9]. Consequently an effort was made to discover some method which would supply more accurate information about the power of localization, and also provide measurable results. The method found to be most serviceable and practicable was a slight modification of that described as Henri's, but, unfortunately, it has not been possible for me to procure the original description of his method. The patient, having the part to be tested obscured from his vision, marked upon a life-sized diagram the position of the point judged to be stimulated, whilst the observer recorded on another similar diagram the exact point touched. After a sufficient number of points had been localized, the two diagrams were superimposed and the two points recorded in each test were marked on one diagram—in different colours or by distinctive signs, and then the error in each case was measured off with a millimetre scale. From these measurements, if a sufficient number of points had been localized, the average error for the whole or individual parts—as each digit—could be determined. In the latter part of the investigation only one chart was used, the observer recording the exact point stimulated after the person examined had marked the point where he felt the stimulation; and this simpler procedure proved as successful, and apparently as reliable, as the more tedious original form.

Using this method, which possesses the great advantage of giving measurable results, the following experiments were performed:—

Experiment 1.—This series, in which ten members of the medical profession provided the subjects for examination, was undertaken at the outset for two principal reasons. In the first place it was thought that any possible fallacy due to unfamiliarity with the diagrams would be reduced to a minimum; and, secondly, such a series would provide valuable information with regard to the introspective aspect of this form of sensation. The tactile pressure was made by a blunt instrument about 0·2 cm. in diameter. The palmar and dorsal surfaces of each hand and digit were explored in turn. Twelve stimulations were made on each surface, eight or nine of which were on the digits and the rest on the palm or dorsum of the hand. The average error for the ten subjects was found to be 0·6 cm. for the palmar and 0·5 cm. for the dorsal surfaces of the right hand and fingers, and 0·5 cm. for both surfaces of the left hand and fingers.

Experiment 2.—In this series, ten non-medical people were examined and only the palmar surface of the two hands and digits explored. The ten were composed of clerks, departmental stewards, porters, and second-year students. The same number of stimulations were made, and the same proportion on the hand and digits, by the same instrument as in the previous experiment. The average error for the ten was 0·6 cm. for the right hand and 0·7 cm. for the left. The close similarity in the results in the two experiments is rather remarkable, and shows that any error due to unfamiliarity with the charts, at any rate for the palmar surface of the hand and digits, must be very slight. This conclusion was confirmed by a large series of tests carried out upon pensioners under my charge, in whom an average error of 0·6 cm. was found for the palmar surface of the hand and digits on both sides.

Experiment 3.—This series was undertaken to discover the normal average error for the individual fingers and to find out if there was normally any definite variation in the power of localization in the different fingers. Two people were chosen from each of the former experiments and twelve pressure stimulations (six on the palmar and six on the dorsal surface) were made on each finger of right hand. As far as possible two stimulations were made on both surfaces of each segment of a finger.

The average error for the four persons examined was found to be 0·4 cm. for the index, middle, and ring fingers, and 0·3 cm. for the little finger; from which it appeared that the power of localization did not vary to any obvious extent in the four fingers.

Further details and tables showing individual errors in these three experiments are given in the paper previously referred to.

Experiment 4.—From the results which were being found on applying this test to patients suffering from division of peripheral nerves, it was decided to perform a series of tests using as a stimulus a hair, which could not possibly stimulate any but cutaneous nerve terminals. For this investigation three medical people were chosen from those used in Experiment 1 and a similar number from the non-medical group of

Experiment 2. The same number of stimulations were made with the hair as in the former experiments where pressure had been used as the stimulus, and the conditions under which the tests were performed were identical with those of the previous experiments. It was found that a purely cutaneous stimulus could be localized very accurately; in Table II the results are compared when using a hair and when using pressure with an instrument 0·2 cm. in diameter. The latter records had been taken some weeks previously.

TABLE II.

	Right Hand			Left Hand	
	Hair	Pressure		Hair	Pressure
SL.	·5 cm.	·4 cm.	..	·7 cm.	·6 cm.
SJ.	·5 ,,	·7 ,,	..	·7 ,,	·5 ,,
EAL.	·6 ,,	1·0 ,,	..	·5 ,,	·8 ,,
AFCD.	·5 ,,	·5 ,,	..	·4 ,,	·6 ,,
AG.	·6 ,,	·7 ,,	..	·7 ,,	·7 ,,
RF.	·5 ,,	·5 ,,	..	·5 ,,	·5 ,,
Average	·5 ,,	·6 ,,	..	·6 ,,	·6 ,,

From these results it will be seen that accuracy of localization is practically the same, for either a purely cutaneous stimulus or pressure, in individuals with normal sensation.

It is of interest to notice that in the observations made upon Head's hand [5], it was found that accurate localization of cutaneous stimuli did not return until the skin was sensitive to tactile hairs after shaving.

Experiment 5.—After the former more or less preliminary experiments, which were undertaken chiefly to gain experience and establish the normal degree of error in localization, had been carried out, the pressure test was applied to twenty patients who were known from surgical observations to have suffered from division of one or two peripheral nerves of the upper limb at various levels. A similar number of stimulations as in Experiments 1 and 2 were made over the region of the cutaneous distribution of the affected nerve and, for comparison, on the normal part of the same hand or a similar region on the unaffected hand. Stimulations were made with the same instrument as that used in the other experiments. In ten patients, the observations were taken shortly after the performance of secondary suture of the injured nerve, at a time too early for any regeneration to have occurred. The results are tabulated in Table III.

The average error for the ten patients over the cutaneous field of the sutured nerve was 1·4 cm., whereas on the normal part it was 0·6 cm.

TABLE III.—LOCALIZATION (PRESSURE) TESTS, AFTER COMPLETE NERVE DIVISION AND SUTURE AT A TIME WHEN NO REGENERATION HAD OCCURRED.

Patient	Nerve	Site of suture	Average error for localization over area of epicritic loss	Average error for localization over normal area
T. E.	Median	Upper forearm	1·2	·6
J. D.	Median	Middle of forearm	1·4	·5
H. S.	Musculo-spiral	Elbow	1·1	·4
T. M.	Ulnar	Middle of forearm	1·7	·7
A. M.	Median	Middle of forearm	1 0	·5
N. D.	Ulnar	Middle of forearm	1·2	·4
J. J. T.	Median	Arm	1·8	·6
A. L. B.	Ulnar	Elbow	1·1	·6
J. T. S.	Ulnar	Lower forearm	1·9	·8
F. S.	Ulnar	Middle of forearm	1·2	·8

In the case of T.M. two stimulations on the little finger had to be left out of the calculations since he said he was unable to place them; he knew one was "somewhere" on the little finger, but the other seemed "somewhere" on the inner part of the hand.

In seven other patients the investigation of localization was made after protopathic sensibility had made a complete recovery, but before there was any reduction in the loss of epicritic sensibility. The results of this set are recorded in Table IV.

TABLE IV.—LOCALIZATION (PRESSURE) TEST, AFTER COMPLETE NERVE DIVISION AND SUTURE, WITH RECOVERY OF PROTOPATHIC SENSIBILITY AT TIME OF OBSERVATION.

Patient	Nerve	Site of suture	Average error for localization over area of epicritic loss	Average error for localization over normal area
B. K.	Median and ulnar	Wrist	1·4	·9
A. N. K.	Ulnar	Elbow	1·4	·5
S. O.	Ulnar	Middle of forearm	1·4	·5
J. R. M.	Ulnar	Upper forearm	1·6	·5
O. R.	Median	Middle of forearm	1·4	·8
V. P.	Ulnar	Lower forearm	3·0	·5
T. T. P.	Median	Lower forearm	1·1	·5

The average error for the seven patients over the area of epicritic loss was 1·6 cm. and over the normal part 0·6 cm. This series shows that the error in localization is not diminished during the recovery of protopathic sensibility. In two additional patients considerable time had elapsed since the performance of the suture and some recovery of epicritic sensibility had occurred, as well as the return of protopathic sensibility. In both patients gross errors were found with the compass test over the cutaneous distribution of the nerve, although this was sensitive to the lightest application of a camel hair-brush. The findings of these two patients are shown in Table V.

It is of great interest to notice that in both patients the remaining deficiency in sensation affected discrimination, localization, and the recognition of posture and passive movement in the joints supplied by the nerve.

TABLE V.—LOCALIZATION (PRESSURE) TEST, AFTER COMPLETE NERVE DIVISION AND SUTURE, WITH RECOVERY OF PROTOPATHIC AND PARTIAL RECOVERY OF EPICRITIC SENSIBILITY AT TIME OF OBSERVATION.

Patient	Nerve	Site of suture	Average error for localization over area of partial epicritic loss	Average error for localization over normal area
W. H.	Ulnar	Arm	1·0	·7
T. N. W.	Median	Upper forearm	1·3	·9

In one other patient the only evidence of any regeneration of afferent fibres was a slight recession of protopathic loss, although four years had elapsed since the time of the secondary suture of the median, and the error in localization for the anæsthetic area was 1·2 cm., whereas for the normal part it was 0·4 cm.

By the application of this method of testing localization, which gives measurable results, to patients known to be suffering from division of peripheral nerves, it is shown that, contrary to the present view, accurate tactile localization is not present even when the pressure is sufficient to stimulate the deep afferent system. It is difficult to decide whether the defective power of localization in these twenty patients was due to loss of cutaneous or subcutaneous nerve terminals, or both, since pressure may stimulate both, and although in eighteen of the patients the skin was anæsthetic, we have no accurate anatomical or physiological information about the fibres of the median or ulnar distributed to subcutaneous tissues.

Experiment 6.—Head [5] has stated that "localization is in all probability the sum of two sets of sensation, one of which arises from deep, the other from cutaneous stimulation." The foregoing experiments are in perfect agreement with this contention, but it is difficult to decide whether the errors in localization in Experiment 5 were due to the loss of cutaneous sensation only, or to a disturbance of the deep system in addition. The power of localization which remains, in the patients used in Experiment 5, must be entirely dependent upon the deep system, but for the anatomical reasons stated in an earlier section, we cannot claim that it represents the normal power of localization served by fibres terminating in subcutaneous tissues. In an endeavour to arrive more closely at a correct conception of the part played by the cutaneous and deep systems, several preparations were applied to the unbroken skin in an attempt to obtain an uncomplicated cutaneous anæsthesia. None of these gave a satisfactory anæsthesia, until on the suggestion of my colleague, Professor R. B. Wild, a 10 per cent. solution of cocaine hydrochloride in chloroform was used. With this it was generally found practicable to get an almost complete cutaneous anæsthesia of a small area in about ten to fifteen minutes. The solution was applied to the dorsum of the left index finger in three of the subjects used in Experiment 3. When the skin was found, by testing with a wisp of cotton wool, to be satisfactorily anæsthetized the examination of localization was made by eight pressure stimulations. At a later date the normal power of localization of the same part was tested by eight pressure stimulations. The average error for the eight stimulations, in the three subjects with and without cutaneous anæsthesia, are shown in Table VI.

Table VI.

	Normal average error	Average error with cutaneous anæsthesia
S. L.	·3 cm.	·4 cm.
A. F. C. D.	·2 ,,	·2 ,,
S. J.	·2 ,,	·3 ,,

It will be seen that in the three subjects the power of localization was almost as accurate when there was cutaneous anæsthesia as normally. It is only possible to anæsthetize satisfactorily a small cutaneous area and this may be raised as a criticism, but although only the dorsum of one finger was examined the result of the experiment strongly favours the presumptions that :—

(1) Accurate localization is possible through the deep system alone.

(2) Since the errors in localization in the twenty patients examined in Experiment 5 were gross, there was a disturbance of localization through the deep system and the errors were not dependent upon a loss of cutaneous localization.

In several of the patients examined in Experiment 5 the division of the nerve occurred at the wrist or in the lower part of the forearm, and there was an average error of twice the normal. Therefore we may suggest with some confidence that accurate localization through the deep system alone is disturbed by a section of the median or ulnar at the wrist.

V.—Pressure Pain.

To investigate deep sensibility further it was necessary to test that form of sensation which is now well known as pressure pain.

For this purpose an algometer was made for me similar to that used by Rivers [3]. From some preliminary tests with the instrument it became clear that certain technical difficulties in its use were to be overcome, and it appeared necessary to carry out at the outset some experiments upon normal individuals in order to establish a standard procedure when using the instrument upon patients.

Experiment 1.—These preliminary tests were made upon six normal individuals, three on the right hand and three on the left, and in each the pressure was applied at eight selected points which are shown in fig. 2. At each point three readings were taken, and it was soon found

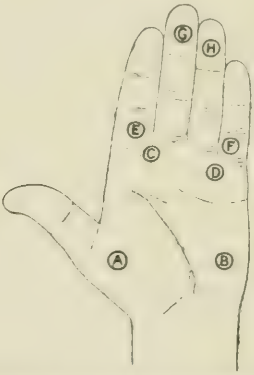


FIG. 2.—To show the position of the eight selected points used in Experiment 1 (pressure pain).

that the second and third readings ought not to be taken over the exact point of the former, since repetition of pressure over the same spot resulted in pain being experienced with much less pressure than on the previous occasion. Inequality in the three records in the same neighbourhood was found to be due to differences in the rate of application of the pressure; it was therefore necessary to apply the pressure evenly and slowly, which is by no means easy, and some of the greater differences in the three readings may be due to this cause. A third cause of difficulty was due to the personal factor, as it was not always possible to get the person examined to indicate at once the onset of the painful element in the sensation aroused by pressure. In the first series, several informed me that there was a great tendency to compare a second experience of pain with the first, which tended to disturb their judgment. These sources of fallacy make it important, as Head as already stated, to take at least three readings at each point.

The results of the investigation of the six normal individuals are given in the Table VII, which shows all the three readings at each of the eight points.

TABLE VII.—TO SHOW THE AMOUNT OF PRESSURE REQUIRED TO INDUCE PAIN, AT EIGHT SELECTED POINTS ON THE HAND AND DIGITS, IN SIX NORMAL INDIVIDUALS.

	A	B	C	D	E	F	G	H
S. J.	2·50	3·25	1·50	1·25	3·00	2·50	1·00	·75
	2·75	3·00	1·25	1·25	2·00	2·50	·75	·75
	2·50	3·50	1·25	1·50	2·50	2·50	1·25	1·00
G. M. D.	2·50	2·50	1·50	·50	2·25	2·00	·50	·25
	2·00	2·25	1·25	·50	1·00	1·50	·75	·25
	1·75	1·75	2·00	·75	1·25	1·75	·25	·25
D. S.	2·75	2·00	1·25	1·00	1·00	1·00	·25	·5
	2·00	2·50	1·00	·75	1·25	·75	·25	·75
	1·00	2·50	·75	·75	1·50	·75	·25	·25
R. F.	2·25	2·25	1·25	1·00	1·75	2·00	2·00	1·75
	2·25	1·00	1·50	1·25	1·75	1·50	2·25	·50
	1·75	1·75	1·00	1·00	1·50	1·25	1·75	1·25
L. S.	1·50	2·00	·75	1·00	1·25	·75	·50	·25
	1·75	2·00	·75	·50	1·50	1·50	·50	·25
	1·75	1·50	·75	1·00	·75	1·25	·25	·50
H. G.	2·75	3·50	1·50	2·25	2·75	2·50	2·25	2·25
	2·50	3·00	1·50	2·25	2·50	2·75	2·00	2·25
	2·75	3·25	2·25	2·75	2·75	2·75	2·00	2·25

The results of this experiment brought out the following information:—

(1) Greater pressure was usually required to produce pain in the thenar and hypothenar regions than at the other points tested.

(2) Less pressure was required at the base of the clefts between the fingers than over the palmar surface of the proximal segment of the digits. This is presumably due to the exposed position of the digital nerves as they divide in the region of the clefts into branches for the adjacent sides of the neighbouring fingers.

(3) With a single exception, less pressure was needed to induce pain over the palmar surface of the distal segment of a digit than over its proximal segment.

Experiment 2.—With the knowledge and experience gained from this preliminary investigation of pressure pain, the test was applied to a number of patients suffering from division of the median or ulnar nerves. To simplify the presentation of the results of this experiment only the average of the three readings at each point is recorded, and for ease of comparison the results of five typical tests are represented in a diagrammatic form (figs. 3, 4 and 5). As in the former experiment the pressure required to induce pain is recorded in kilogrammes.

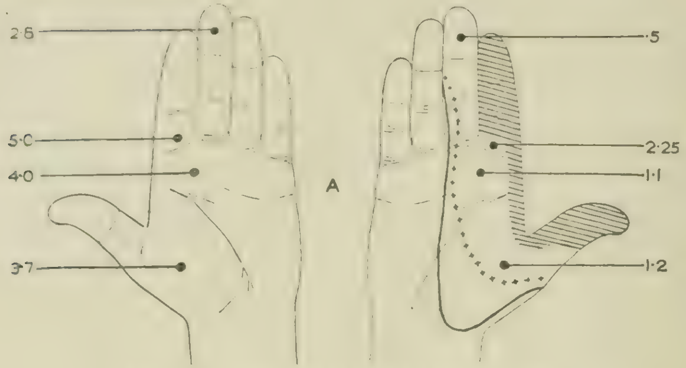


FIG. 3, A.—Division of median nerve in arm.

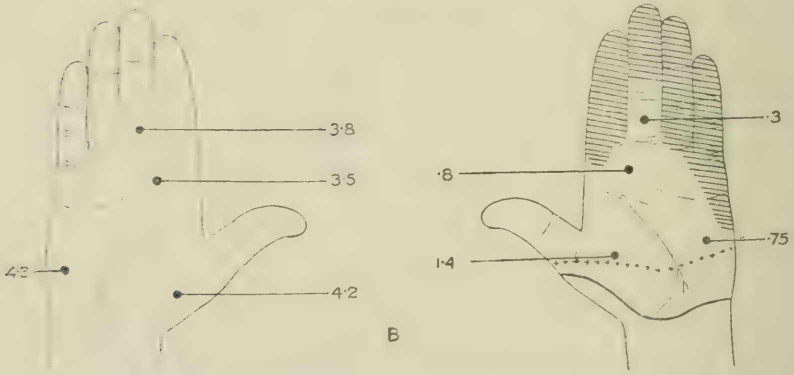


FIG. 3, B.—Division of median and ulnar nerves in arm.

Crosses = analgesia to prick of pin.
Thick line = anæsthesia to lightest applications of fine brush.
Shading = complete sensory loss.

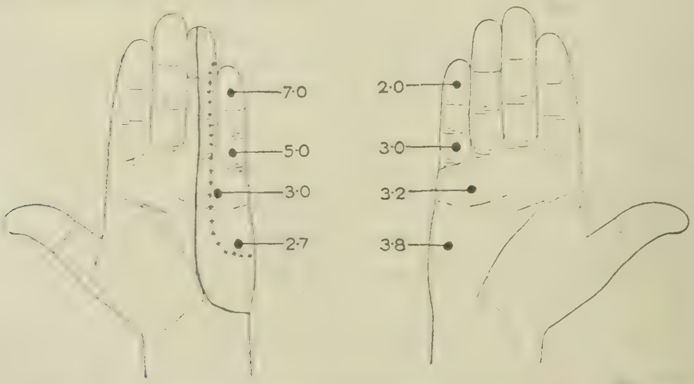


FIG. 4.—Division of ulnar nerve in upper forearm.

Crosses = analgesia to prick of pin.
Thick line = anæsthesia to lightest applications of fine brush.

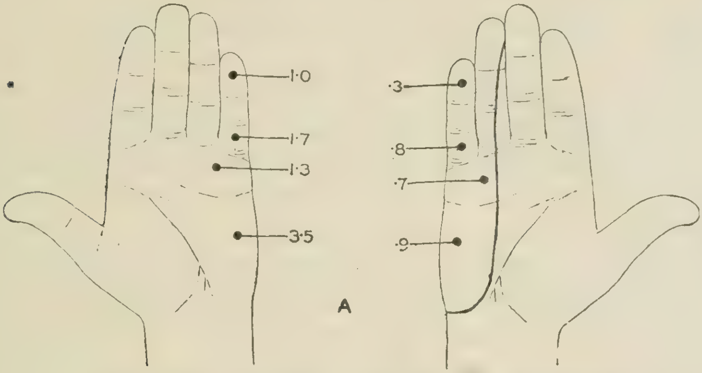


FIG. 5, A.—Division of ulnar nerve in lower forearm.
Thick line indicates anæsthesia to lightest applications of fine brush.

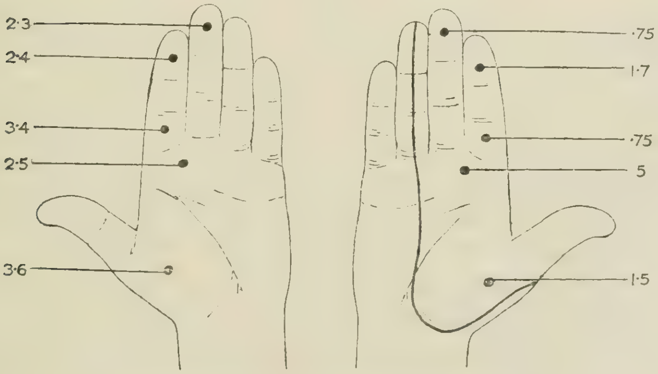


FIG. 5, B.—Division of median nerve in arm.
Thick line indicates anæsthesia to lightest applications of fine brush.

By these experiments it was found :—

(1) That it was distinctly easier to test pressure pain on the abnormal than on the sound side. This was due to the fact that when testing over an area where epicritic sensibility was lost, the patients could more readily recognize the onset of the painful element since it commenced abruptly and rapidly became intensely painful. Several patients told me that they had no doubt on the affected side, whereas on the sound side they were often in difficulty as to when the pressure became actually painful. As Head found, several expressed fear at the application of pressure on the affected side, and this, together with the

experience that on this side the pain quickly became intense, may have caused in some of the tests an abnormally low reading on the affected side.

(2) In those patients where the division of the nerve was in the distal part of the limb and there was no absolute sensory loss, the readings on the affected side tended to be definitely lower than on the sound side.

(3) In some patients with division of the median in the middle of the forearm, i.e., proximal to the supply of that portion of the flexor sublimis digitorum which flexes the index finger and distal to the origin of the anterior interosseous nerve and branches for the supply of the main flexor mass, considerably more pressure was required on the index on the affected than on the sound side. These results pointed to a disturbance, but not complete loss, of this form of sensation in the index after division of the median proximal to the origin of the most distal branch to the flexor sublimis digitorum, and indicated that some fibres for this form of sensation in the index were transmitted by this muscular branch, and probably extended to the digit along the tendon. Similarly, after division of the ulnar in the upper part of the forearm, although the inner part of the flexor profundus digitorum was capable of voluntary action, higher readings were sometimes found on the little finger on the affected side than on the sound side. It is not so easy to give an anatomical reason for this occurrence, which is found only in a proportion of cases of division of the ulnar in the forearm and is nothing like so constant as the similar condition just described in the case of the median, but it may be due to the occasional appearance of an extra branch to the flexor profundus digitorum in the lower part of the forearm.

The associated demonstrable disturbance of the appreciation of contact in these cases will be referred to in the next section.

(4) In the patients examined during recovery, when there was a complete return of protopathic sensibility (fig. 5), the readings at all points on the affected side were lower than on the normal side. This was found even over digits that at the outset had exhibited an absolute sensory loss, or which originally had given a higher reading. These results indicate that the recognition of pressure pain returns at an early stage in recovery, at the same time as protopathic sensibility. It is also significant that in cases of only partial recovery of sensation pressure pain like protopathic sensibility is one of the most constant to manifest some improvement.

VI.—RECOGNITION OF THE "CONTACT" OF TACTILE PRESSURE.

In routine examinations of patients suffering from injury to, or disease of, the peripheral nerves, this aspect of deep sensibility is usually the only one tested. Consequently if the patient appreciates everywhere the contact of some instrument, as the head of a pin, "no loss of deep sensibility" is generally recorded in the notes. It does not seem to have been realized previously that the various forms of sensation grouped together as deep sensibility may be dissociated, and this, together with the widespread belief that deep sensibility is practically entirely transmitted by afferent fibres which run with motor nerves and reach their termination by accompanying such structures as long tendons, has been responsible for the confidence with which observers have been content to investigate simply the recognition of contact as the standard test for deep sensibility.

As is to be expected this form of deep sensibility is only appreciably affected in lesions in the proximal part of the limb, i.e., above the origin of the supply of branches to the long flexors of the digits. There is no doubt that mere recognition of contact is chiefly transmitted by afferent fibres which run in the branches to the long flexor muscles of the digits. In this respect it is instructive to refer to the fairly constant occurrence of complete anæsthesia of the distal part, and sometimes the whole of the palmar surface of the index finger after complete division of the median in the middle third of the forearm, although the division occurs distal to the origin of the main branches supplying the flexor sublimis digitorum and the anterior interosseous nerve. This is apparently due to the origin from the median trunk in the lower third of the forearm of a branch which supplies that portion of the flexor sublimis digitorum which flexes the proximal interphalangeal joint of the index finger. From a study of the number of patients with division of the median in the upper part of the forearm, where the precise anatomical level with regard to the origin of branches had been defined at operation, I am inclined to the view that a greater proportion of afferent fibres pass in the branches to the flexor sublimis digitorum than to the flexor profundus digitorum.

From personal observations it seems to be almost a rule that if any power to appreciate contact is retained in a part there is always in the same region some retention of the power to recognize pressure pain, although the amount of pressure required to induce pain may be very much greater than in the same region on the sound side. This latter point is well illustrated by the following record, which also supports the previous contention that more afferent fibres are transmitted by the tendons of the flexor sublimis digitorum than those of the flexor profundus digitorum.

Patient, J. C. Complete division of the ulnar was found in the upper part of the forearm, just distal to the origin of branches for the supply of the flexor carpi ulnaris and inner half of the flexor profundus digitorum, which muscles possessed voluntary power. The loss of epicritic and protopathic sensibility corresponded to the full typical normal distribution. It was impossible to measure the error in the localization of tactile pressure over the little finger, as the best response to any stimulation he gave was "somewhere on my little finger," and he was quite unable to attempt to chart any of the stimulations in this region, although he invariably recognized that a contact had been made, provided sufficient pressure was used. The average of the three readings with the algometer on the two sides at four points may be conveniently tabulated for comparison.

	Sound side		Affected side
Hypothenar region	3·8	..	2·7
Between heads of 4th and 5th metacarpal bones	3·2	..	3·0
Over proximal phalanx of little finger ..	3·0	..	5·3
Over distal phalanx of little finger	2·0	..	7·0

It will be noticed that in the first two regions the reading was slightly lower on the affected side, whilst in the case of the two tests on the little finger the reading was markedly higher on the affected side, being more than three times greater on the distal phalanx.

Two other patients in whom similar results were found have been encountered. I have never seen "contact" and "pressure pain" completely dissociated. On the other hand these two forms of deep sensibility may be retained in a part without any power of localization being present, as in the little finger of the patient just referred to.

After division of the ulnar nerve at any point proximal to the origin of the branches for the supply of the flexor profundus digitorum, the area in which complete anæsthesia to all stimuli is found is very constant in extent and affects the little finger and the inner border of the hypothenar region as shown in fig. 6. After division of the median above the level of the branches supplying the long flexor muscles, the area of complete anæsthesia is by no means so constant. In sixteen cases of known complete division of the median, at or proximal to the level of the elbow joint, there was complete anæsthesia only of the index and a small neighbouring portion of the palm (fig. 7, A) in six; of the index and medius and a larger portion of the palm in five (fig. 7, B); and the index, medius and palmar surface of thumb together with a still larger extent of the palm in five (fig. 7, C). The infrequency (only five out of sixteen) of complete anæsthesia of the palmar surface of the thumb was rather surprising, but the foregoing results were confirmed by the examination of a group of patients suffering from

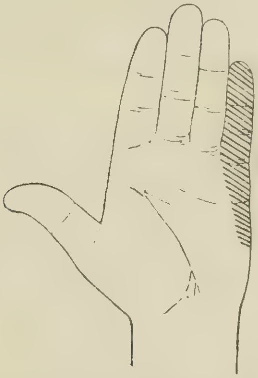


FIG. 6.—To show the typical extent of absolute sensory loss after division of the ulnar nerve in the arm.

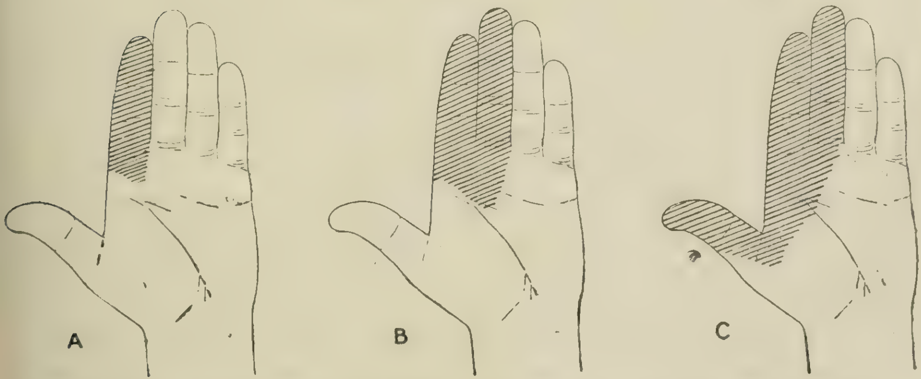


FIG. 7.—To show the variation in extent of the absolute sensory loss after division of the median nerve in the arm.

division of both the median and the ulnar nerves in the upper arm, in whom contact (if sufficient pressure was made) was recognized over the palmar surface of thumb in an even higher proportion. Consequently it must be surmised that the radial nerve, and possibly in a small number the musculo-cutaneous, by means of perforating branches, takes part in the innervation of the deeper tissues of the palm and the palmar surface of the thumb.

VII.—Summary and Conclusions.

In each section the main conclusions which may be drawn from the experiments and investigations are presented; it now only remains necessary to restate the principal conclusions bearing upon our present conception of sensation, and these may be conveniently summarized in three divisions.

(1) It seems clear that no nerve of sufficient size to be of clinical importance, or to be selected for experimental work upon sensation, is distributed exclusively to skin. Consequently after section of any of the nerve trunks, even in the distal part of a limb, there is bound to be some disturbance of so-called deep sensibility, and it seems quite impracticable to divide sensation into superficial and deep. Besides this anatomical criticism of such a division there is to be remembered the additional confusion which may arise from the knowledge that one form of sensation at least is transmitted by both cutaneous and deep nerves. It has been proved that so-called deep sensibility is not transmitted entirely by nerve fibres which accompany muscular branches, since the sensory supply of the joints of the fingers and thumb undoubtedly arises from the digital nerves, and it seems probable that other forms of deep sensibility are in part, at least, transmitted by branches arising independently from the main nerve.

(2) The various forms of sensation included under the division of deep sensibility may be dissociated. After division of the median at the wrist there is found a loss of the recognition of passive movements at the metacarpo-phalangeal and interphalangeal joints of the digits supplied by the nerve: some power of localization is retained over the region of the cutaneous distribution of the nerve, although by means of a measurable test a gross error is seen on comparing the results with those obtained on the normal part; the least pressure is readily recognized everywhere, and the readings with an algometer show that rather less pressure is required to induce pain on the affected than on the sound side. If division of the median occurs proximal to the supply of the outer part of the flexor sublimis digitorum in the lower third of the forearm, in addition to the defects just recorded there is usually a complete sensory loss to all forms of stimulation over the distal two segments, or the whole of the index finger. In a small

proportion after section of the median at this level the loss of sensation in the index finger is less profound. Although in these there is no power to localize, the contact of pressure can be recognized and pain can be induced by excessive pressure, but on investigating the two latter forms of sensation more fully it is discovered that more pressure is required to induce the sensation of contact over the index than the medius and the reading with the algometer is considerably higher than on the sound index. The condition of what we know as deep sensibility in the index is, in such cases, in a most interesting stage and may be summarized as follows :—

(i) Loss of sense of position and recognition of passive movement in all joints of this finger.

(ii) Absolute loss of localization.

(iii) Retention of recognition of contact and pressure pain, but on the application of measurable tests it is found that these forms of sensation are grossly affected.

Little reference need be made to the effect upon deep sensibility of a lesion at a higher level, in the region of the elbow or in the arm, since, except with regard to localization which has already been fully discussed, the condition is well known ; reference is only necessary to the fact that the extent of the absolute sensory loss to all stimuli is variable.

(3) Observations upon the recovery of deep sensibility demonstrate several striking and significant features. Reappearance of the recognition of contact and appreciation of pain on the application ot excessive pressure occurs early, as a rule during the stage of protopathic recovery. At first considerable pressure is required before it is appreciated, but the recovery of contact without concomitant recovery of pressure pain has never been encountered, although the extremely high reading with the algometer in two patients examined suggest that this is possible, and there does not appear to be any obvious reason why these two forms should not be dissociated. As regeneration proceeds less pressure is found to be required at subsequent examinations. As the recognition of contact and pressure pain improve there is usually a return of some power of localization, but it is very grossly defective, the error being much greater in regions where there has previously been an absolute sensory loss than elsewhere. Further improvement in localization and signs of recognition of passive movement of joints occurs very late, and not until there is evidence of recovery of epicritic sensibility. Most of my studies have

been upon patients who have had a secondary suture of the median or ulnar nerve, and under these circumstances any recovery of accurate localization or recognition of passive movements of joints is at the best very defective and frequently remains absent. After primary suture there is a better opportunity for studying the later phases of recovery. It seems very significant that recovery of recognition of contact and appreciation of pressure pain, followed often by a gross and defective return of the power of localization, occur early during the stage of reappearanee of protopathic sensibility, whilst accurate localization and recognition of passive movement only appear late, at a time when there is also evidence of epicritic return as tested by graduated hairs and the compass. That is to say the three forms of sensation concerned with spacial recognition—accurate localization, discrimination and recognition of passive movement—only recover at a very late stage, and even after primary suture are apt to remain defective.

These observations upon the recovery of certain forms of sensation after suture of a peripheral nerve suggest two important facts.

(*a*) What we have regarded as deep sensibility ought to have been subdivided, just as cutaneous sensation has been divided, into epicritic and protopathic. There is no doubt that the two forms of sensation, recognition of the contact of pressure and appreciation of passive movement, must be subserved by nerve fibres terminating in the deep tissues; the former of these returns early at a time when protopathic sensibility is recovering, whilst the latter returns at a late stage, if at all, during the time of epicritic recovery. The mere recognition of the contact of pressure is a crude form of sensation compared with the more highly graded appreciation of the direction, localization and range of passive movement of a joint.

(*b*) In the light of Head's recent work upon the sensory cortex [2], these results suggest that at the periphery, both in cutaneous and deep tissues, we have cortical and thalamic aspects of sensation. The dissociation which is encountered after the division of any large nerve trunk makes it exceedingly difficult to unravel the fundamental principles upon which sensation at the periphery is based, but when we get an accurate conception of the anatomical distribution, and in the light of this knowledge analyse the results of careful clinical examinations of a number of patients suffering from division of a peripheral nerve, the curious forms of dissociation become more intelligible. Continued examinations of the same patients during recovery seem to bring us still nearer to a knowledge of the true state of affairs. It has just been stated that certain forms of deep sensibility constantly recover during the early stage when the area of protopathic loss is found to be receding, whilst other forms do not show any recovery until a late stage when there is clinical evidence of a return of epicritic sensibility. In the examinations of a very large number of patients I have found this to be an invariable rule.

It appears to have been generally believed that the earlier return of protopathic sensibility is dependent upon a more rapid rate of regeneration in protopathic than epicritic fibres. Such an explanation supposes some structural difference in the two systems, and Ranson [4], on histological and experimental evidence, made the suggestion that impulses giving rise to pain travel in non-medullated fibres; but more recent work by Adrian [1] shows that it is highly improbable that there is any definite structural difference in the fibres concerned with protopathic and epicritic sensation. A simpler explanation is suggested when we take into consideration all the forms of sensation which return during the later stage of recovery. The forms appearing late, which more frequently show imperfect recovery, or in quite a proportion of cases of secondary suture fail to recover, are those which Head has proved to have cortical representation; whilst the forms which exhibit early and more constant recovery are those which may be expected to persist after destruction of the sensory cortex. Therefore it seems more reasonable to expect to find an explanation of the two stages of recovery in the central nervous system, rather than to find it due to a different rate of regeneration of two sets of fibres which anatomically appear to be identical. After suture and regeneration of a peripheral nerve a much longer period may be expected to elapse before the fibres subserving cortical forms of sensation function correctly, than in the case of the fibres conducting the thalamic aspects of sensation; since a very much more complex readjustment and re-education must occur after regeneration of the fibres in the former case than in the latter. Furthermore, on the hypothesis suggested in this paragraph, we seem to have ample reasons for the more constant and perfect recovery of such aspects of sensation, as cutaneous pain, pressure pain and appreciation of extremes of temperature, than for the higher forms, as those concerned with spacial recognition.

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TOXIC POLYNEURITIS.[1]

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Recognition of multiple or peripheral neuritis as a clinical and pathological entity dates from the publications of Duménil in 1864 [10] and especially of Leyden in 1880 [24]. Since that time a host of observers have studied the disease, so that the varieties of the commoner forms, the alcoholic, lead, arsenical and diphtheritic paralyses, are well known. It is not my intention to dwell on those forms the etiology of which is clear and unmistakable, but rather on the numerous lesser known types, the origin of many of which is quite obscure.

Multiple neuritis in our present state of knowledge is best classified on an etiological basis, rather than on pathological distinctions or clinical differences, and four main groups may be separated:—

(1) Those dependent on the absorption of poisons introduced into the body.

(2) Those due to autotoxæmia, or to poisons developed primarily within the body.

(3) Those due to infections of an organismal nature.

(4) Those occurring in cachectic states.

The first group may usefully be divided into two sub-groups, those due to metallic poisoning, and those due to poisoning by various carbon compounds.

The term toxic polyneuritis has been much used, but, as probably all polyneuritis is dependent on some toxin, its employment seems most appropriate for those cases in which the infective agent or the source of poisoning is not clearly established. Before dealing with these a few examples of rarer forms from the different groups may be referred to.

Silver is a very rare and probably doubtful cause of polyneuritis, the only case in the literature appearing to be that described by Gowers [13], of a man of 44 who took a dinner pill containing silver for about twelve years, averaging six pills a month. After eleven years cyanosis commenced to develop, and a year later wrist-drop, though as carcinoma of the liver declared itself some three months later, it is possible that the polyneuritis was to be accounted for by the toxæmia from the malignant disease.

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[1] Presidential address delivered before the Neurological Section of the Royal Society of Medicine, October 12, 1922.

Carbon bisulphide is a sufficiently uncommon cause of polyneuritis to justify a short description of a case I have had recently under treatment.

A boy, aged 15, worked at a boot factory at solutioning on rubber soles. He worked in a shed, which was afterwards described by the inspector as very badly ventilated, using for the purpose of fastening on the rubber soles a rubber solution containing carbon bisulphide. He worked from 8 a.m. to 6 p.m., and began to feel unwell in July, 1921, when he commenced to suffer from headaches almost every night towards the end of his work. The headaches were accompanied by vertigo, but had disappeared by the following morning. He informed me that previous workers at the same job had had to give it up on account of similar headaches and giddiness. He, however, stuck to his work, and in January of this year his right leg began to feel weak and to give way when walking towards the end of the day. This improved, and then the right hand grew weak and lost the power of gripping ; this also improved and the left hand became similarly affected. The headaches ceased in January just before the legs began to be affected. There was never at any time pain or numbness, or objective or subjective sensory symptoms. By the beginning of April he began to develop weakness of the dorsiflexors of both feet, being unable to raise the toes off the ground when standing, though the gastrocnemii were strong. Soon also bilateral weakness of the extensors of the fingers and wrists appeared, especially of the right extensor carpi ulnaris. Marked weakness and wasting of the right first dorsal interosseus and thenar muscles was also seen. To electrical testing there was well-marked reaction of degeneration in the extensors in both forearms, in the right first dorsal interosseus and in the tibialis anticus on each side. The knee-jerks were normal throughout, but the right Achilles jerk was absent, and the left only just obtainable with reinforcement. Treated with strychnine injections and massage he soon showed slight improvement, and after four months had practically recovered.

Carbon monoxide polyneuritis I have never met with, but it is said that a single severe dose of poisoning with this agent may be followed by neuritis, a very unusual feature in polyneuritis, which is usually the sequel of a more sustained or chronic poisoning. Care must, however, be taken in cases of carbon monoxide poisoning not to mistake pressure neuritis of the musculo-spiral, external popliteal or other nerve trunks for toxæmic neuritis, pressure palsies being especially liable to occur in persons rendered unconscious by coal gas poisoning or by explosions in coal pits, through lying on a hard surface in one position for many hours.

Rheumatic polyneuritis.—Acute rheumatism or rheumatic fever is rarely if ever followed by polyneuritis, yet local perineuritis and fibrositis, as seen in brachial neuritis and sciatica, are common sequelæ of chill and exposure, though other causes frequently contribute, such as dental or intestinal sepsis.

Chloretone has been given extensively in children for chorea, and has been observed to produce a condition of flaccid paralysis, with absent deep reflexes, but the recovery on cessation of the drug is usually much more rapid than is usually met with in other forms of polyneuritis.

Local *asymmetrical neuritis* of definite nerve trunks rather than a symmetrical polyneuritis, is also a feature of typhoid and paratyphoid infections. Thus, a man of 29 with paratyphoid, a week after admission to hospital developed severe pains in the upper arms and shoulders, which kept him awake, followed by marked paresis of the right serratus, latissimus, triceps, and extensors of the right fingers and thumb, and of the left deltoid.

Another case of asymmetrical severe neuritis of the right median, ulnar and musculo-spiral nerves occurred in a man aged 27, as the sequel of a febrile attack of uncertain origin with tonsillitis, followed by acute nephritis. There was never any peeling of the skin to suggest scarlet fever, and bacteriological examinations for diphtheria, enteric and paratyphoid were negative. Possibly the infection was rheumatic, as nephritis is one of the rarer complications of this disease. After two weeks he had severe pains in the right arm from the shoulder to the hand, completely losing the use of the arm, and anæsthesia of the hand up to the wrist. The hand became very clawed and atrophic, and the finger pads and skin wasted, but practically complete recovery took place in two years. These asymmetrical forms of toxic neuritis are generally painful, perhaps owing to the inflammatory nature of the lesions affecting the interstitial tissue of the nerves, whereas in the symmetrical polyneuritis without sensory phenomena the lesion is probably purely a parenchymatous degeneration of the nerve elements themselves.

Asymmetrical neuritis of toxic origin may occasionally be met with in chronic alcoholism and diabetes. Musculo-spiral paralysis I have many times seen occur in chronic alcoholism, when the element of pressure could apparently be excluded as a cause. In none of these cases of musculo-spiral palsy was pain a feature of the case, but in the sciatic and external popliteal paralyses met with in diabetes severe pain may be a prominent feature, preceding and accompanying the paralysis. It is difficult to understand how a local asymmetrical neuritis can be set up by the action of a circulating toxin, which should presumably act equally and symmetrically on both sides. The fact that certain whole nerve-trunk areas are liable to be affected in the asymmetrical forms is suggestive of a local interstitial neuritis being present rather than a degenerative parenchymatous neuritis, and this is further supported in my opinion by the fact that these asymmetrical forms are usually intensely painful. It is possible therefore, if not indeed probable, that the circulating toxin is not the direct factor in the development of the neuritis, but that it has led to the local appearance of an inflammatory interstitial neuritis, such as may result from chill and other so-called rheumatic processes.

The actual nature of the circulating toxin in such apparently simple cases as alcoholic or diabetic multiple neuritis is obscure. In all probability it is not alcohol itself or derivative ethers circulating in the blood that sets up alcoholic neuritis, or this disease would surely be commoner than it is, but rather a secondary auto-toxæmia produced by the action of the chronic alcoholism upon the tissues, notably on the digestive tract and the liver. Similarly in diabetes it can scarcely be the direct action of hyperglycæmia on the nervous structures that sets up local or multiple neuritis, nor is it due to acetone or diacetic acid, as both of these substances may be absent in cases of diabetic neuritis. Probably the neurotoxin in diabetes is of the autotoxæmic deficiency type, as will be referred to later.

The polyneuritic psychosis described by Korsakow [22] as common in chronic alcoholism with polyneuritis is certainly met with in other forms of polyneuritis, as Korsakow himself showed, and must therefore not be accepted as evidence that alcoholism is the cause of an obscure polyneuritis. Some two years ago I had the opportunity of watching throughout to its fatal ending a case of polyneuritis of unknown origin, in which the delusions and characteristic disorientation of time and space familiar in Korsakow's psychosis were very marked.

A man, aged 55, hall porter, early in September, 1920, began to suffer from severe pains in the left hip. After a fortnight he had to give up his work, and three weeks later pains appeared in the right hip. On October 16, he was admitted under my care into St. Mary's Hospital as a supposed case of sciatica. There was some loss of power in both legs, and tactile anæsthesia of the feet and ankles, but no loss of power or of sensation in the arms or hands. Both knee-jerks and Achilles-jerks were absent, the plantars flexor. No glycosuria or albuminuria. Wassermann test of blood and c.s.f. both negative. On October 26, the electrical reactions were normal, but on November 5, definite reaction of degeneration had appeared in the left dorsiflexors, and peronei in both legs. By November 12, bilateral foot-drop was well marked, and there was retention of urine, daily catheterization being necessary. His mental condition had gradually become unreliable, and by this date delusions were very marked; he muttered to himself, and replied in the most extravagant manner to questions as to where he had been recently, such as to New York yesterday, and to Jerusalem the day previously, though he would otherwise answer questions quite rationally. He had always consistently denied the imputation of alcoholism, and I was able to convince myself by personal interviews with his wife and with his fellow employees at the Town Hall where he was porter, that his statements on this point were true. Irregular pyrexia developed towards the end of October, and he steadily got weaker and more torpid, dying on December 14. No post-mortem was permitted.

In another case, a man, aged 45, had a severe attack of polyneuritis, with intense pains in his feet and legs, with loss of the deep reflexes, and considerable delirium. Alcohol as a cause could be excluded. He later recovered all his muscular power, and the knee-jerks returned, but there was considerable permanent loss of memory and mental power, indicating the co-existence of an acute encephalitis with the polyneuritis.

Septicæmia is a not uncommon cause of multiple neuritis, differing little in type from alcoholic neuritis. The source of infection may be a quite insignificant wound ; in two cases I saw well marked multiple neuritis follow slight local suppuration due to a grazed skin wound of the hand, and in another case due to a stab wound in the thigh. In one of them an early symptom was loss of ocular accommodation, which is such a common early symptom in post-diphtheritic neuritis.

Septicæmia is a not uncommon cause of multiple neuritis following childbirth or a miscarriage; one of the most severe and painful cases I have ever seen, ending in death from heart failure, occurred in an otherwise healthy girl of 23, after a miscarriage at three months, in all probability an artificially induced abortion. The polyneuritis which has been described as following tetanus is almost certainly of septicæmic origin, rather than due to tetanus toxin, though chloretone used in the treatment has been blamed in one case. I have seen the use of antistreptococcic serum followed by a severe external popliteal paralysis ; a gunshot wound necessitated amputation of the foot, but on account of sepsis three doses of antistreptococcic serum were given on three successive days, and then after four days interval another dose. General joint pains all over resulted, followed four days after the last injection by pains in the right leg, dropped foot and wasting of the leg, with total paralysis of the extensor longus digitorum and of the peronei. It is doubtful whether this was septicæmic neuritis, or an effect of the serum.

Septicæmic neuritis may affect a nerve trunk close to the intervertebral foramina, as in a case of a gunshot wound of the left arm, followed four weeks later by pains in the opposite arm and right side of the neck, with paresis of the right serratus magnus and winged scapula, and hypo-æsthesia of a cutaneous strip from the ball of the thumb along the outer forearm and up to the shoulder, suggestive of neuritis of the sixth cervical nerve.

Generalized polyneuritis affecting all four limbs, with ataxy and loss of the knee-jerks, has been recorded by Clayton [9] in a soldier treated for typhoid by fifteen injections of 50 c.c. each of antityphoid serum. Here again it may be asked whether the polyneuritis was a result of the serum injections, or was it due to the typhoid toxin? My own view is that the neuritis is not the result of the serum treatment, but of the previous toxæmia, just as polyneuritis following diphtheria, whether treated with serum or not, should certainly be laid to the credit of the diphtheritic toxin.

A rare form of polyneuritis with facial diplegia has been described by Feiling [12] and others accompanying *parotitis* and *uveitis*, or polyneuritis may follow parotitis alone.

Acute febrile polyneuritis, first described by Osler [29], was frequently observed during the Great War, and cases were recorded by Gordon Holmes [21], Bradford [6], and others. The sequence of the polyneuritis to definite malaise and pyrexia places this type definitely in the infective rather than in the autotoxæmic group, though the exact source of the toxin has not yet been determined. Facial diplegia was a common symptom in this type of polyneuritis.

I saw a medical officer, just home from France early in 1919, who complained of pains in the left side of the neck, with soreness to touch, as though bruised, and almost immediately aching appeared in both forearms; three days later insomnia, and the arms became weak and the hands shaky. After three weeks facial diplegia developed, with a feeling of intense depression and malaise, with furred tongue, though no pyrexia was detected at any time.

There was a good deal of pain with hyperæsthesia and tenderness of the backs of the forearms, but no actual muscular paralysis. The knee-jerks were present throughout, and the legs were unaffected. There was never any sensory loss, and recovery was complete after three months.

Syphilis as a cause of polyneuritis is usually included in the cachectic group, but occasionally it undoubtedly acts as an acute infective toxæmia.

A man, aged 30, acquired syphilis in January, 1910. Three months later he developed some ataxy and numbness of the feet, but recovered. In October the numbness and ataxy returned with rapid onset of weakness of legs and arms, but again almost completely recovered under injections of salicylate of mercury. In January, 1911, twelve months after the original infection, weakness and wasting of the hands and feet began, which steadily progressed to complete paralysis of all muscles below the knees, with bilateral finger-drop and wasting of the forearm muscles.

All the deep reflexes were lost, but there was no trace of anæsthesia.

By November, 1912, he was recovering fair power in the gastrocnemii, and he could walk fairly with a stick. The hands were now normal, and the knee-jerks had returned, but there was no trace of power in any of the anterior tibial muscles, nor any reaction in them to either form of electrical current. Probably the correct interpretation of this case would be a polyneuritis associated with considerable anterior horn cell damage in the fifth lumbar region.

In considering the etiology of an attack of multiple neuritis in a syphilitic subject, the possibility of arsenical neuritis should not be overlooked if treatment by any of the arsenobenzol preparations has been given.

Tubercle as a cause of polyneuritis has been much discussed, the usual verdict being that such polyneuritis is mainly alcoholic, though the added stress of the tubercular toxin or cachexia, when combined with the chronic alcoholism, much increases the liability to degeneration of the nerves, just as alcohol in addition to arsenic, sepsis with rheumatism, and many other doubly acting causes may combine to produce it. Except when associated with another factor, tubercle is a very rare cause of neuritis. I have seen one case of generalized polyneuritis in a man dying from miliary tuberculosis, with no history of alcoholism or other ascertainable cause.

Tubercular neuritis of the feet.—In two cases of severe and fatal tubercular infection, I have seen symmetrical pains and wasting of the intrinsic musculature of the feet, with glossy skin. The first case had been diagnosed as gout, in spite of extensive pulmonary tuberculosis, by no less an observer than the late Sir William Broadbent in 1895, and remembering this case when I saw the identical condition of the feet seven years later in a woman with obscure renal disease and pyrexia, I confidently diagnosed tubercle as the cause, though no one else agreed with me until the autopsy confirmed this.

In a few cases I have seen tubercular pleurisy followed by intensely severe *brachial neuritis* on the same side, with glossy skin and articular disorganization of the phalanges. Probably this is produced by apical infection of the lung and pleura setting up a secondary inflammatory neuritis in the brachial plexus in its close proximity.

Severe chronic anæmia is usually included among the *cachectic* causes of polyneuritis, though it appears to be much rarer than the spinal degenerations of combined sclerosis met with in conjunction with grave anæmia of pernicious type. I published last year [19] a case of *leukæmic polyneuritis*.

A youth, aged 17, developed well-marked symmetrical polyneuritis, with foot-drop, absent deep reflexes and sensory diminution on the feet and legs, as well as tingling and numbness of the finger-pads. His spleen was enlarged three finger-breadths, but there was no leucocytosis, indeed a leucopenia of only 5,800, but the cell count was notably inverted, the polymorphs being only 23 per cent. and the lymphocytes 68 per cent. Slight enlargement of the glands in the neck appeared, and one of these was removed for pathological examination, but was reported to be normal. Troublesome hæmorrhage from the wound continued at intervals, again suggestive of leukæmia, and he died six weeks after admission into hospital, three months after the first appearance of weakness of the legs.

Microscopical examination of the liver, kidneys and peripheral nerves showed these tissues to be infiltrated with lymphocytes, yet it is difficult to conceive that the symmetrical polyneuritis could be due to pressure of the lymphocytic exudation upon the nerve fibres; it was more probably of toxic origin due to some unknown form of autotoxæmia connected with the leukæmic process.

Malignant disease is also included amongst the cachectic group of polyneuritis, though it seems to be rare.

A year ago I saw a civil engineer, aged 69, who had been operated on seven years previously for malignant growth of the ascending colon, a short circuit being performed. He recovered well, and for years lived an ordinary life, travelling a great deal. In October, 1921, he thought he caught a chill, followed by pains in the left shoulder, arm and forearm, "like a rat gnawing it." The pains spread across the back of the neck and then affected the right forearm, being so severe as to necessitate morphia. When I saw him in December there was complete paralysis of both triceps, and of the extensors of the fingers and ulnar extensors of both wrists, though the radial extensors of the wrists and the supinator longus of each side were normal; both serratus magnus muscles were very weak. There was a large mass in the right hypochondrium, which was shown at operation to be growth in the ascending colon with most extensive involvement of the liver. The legs were unaffected and the knee-jerks brisk; there was no glycosuria.

The distribution of the polyneuritis in this case was most unusual, with bilateral finger-drop and total paralysis of both triceps muscles, the legs being quite unaffected. The intensity and long duration of the pain were also striking features of the case. Possibly chill contributed to the onset of the neuritis, but the duration of three months with increasing symptoms was more suggestive of a continually acting toxin or cachexia, and is better explained by the extensive carcinoma from which he was suffering.

Autotoxæmia.—Perhaps the most interesting group of causes of polyneuritis is that I have labelled "autotoxæmic." We are constantly meeting with cases in which the closest investigation can elucidate no cause for the polyneuritis. One is tempted therefore to look upon them as autotoxæmic, though the Scotch verdict of "not proven" would be more correct.

An unmarried woman, aged 47, a school teacher, early last November began to suffer from burning pains in the legs, the feet becoming numb two months later, with loss of power of walking. There was some swelling of the hands due to rheumatoid polyarthritis, which also involved the left knee-joint. She complained of pins and needles in the fingers, and developed finger-drop owing to paresis of the extensor communis, and weakness and wasting of the intrinsic musculature of the hands. There was tactile anæsthesia and analgesia of the left hand up to the wrist, but no objective loss of sensation on the right hand, though she said it did not feel natural. There was complete left foot drop and some weakness of the right dorsiflexors. She could move the right but not the left toes. Though the right foot was much stronger than the left, there was much denser anæsthesia of this limb, extending to just above the knee. The knee-jerks were both brisk and equal, the Achilles-jerks were absent, and the left forearm flexor jerk absent too, though the right was brisk. After two months the pains in the legs increased considerably, and she complained of a curious subjective sensation "as though she had several pairs of legs in bed." This continued for several weeks. Now, after eleven months, there is some improvement in the muscular power of the legs, but she is still only just able to walk. There was a perforation of the nasal septum, suggestive in appearance of old syphilis, probably congenital, but the Wassermann reaction in the blood was negative.

It was difficult to assign the cause of this polyneuritis, though I incline to look on it as *rheumatic polyneuritis*, in view of the presence of painful multiple joint swellings, and the asymmetry and painfulness of the affection.

Beri-beri was at one time considered to be an infective polyneuritis due to a bacterial poison, but the more recent view ascribes it to a deficiency of vitamines in the diet, due to the eating of polished rice; the husk of the grain, which is thus lost to the diet, containing all the vitamins. Such a deficiency can act indirectly only, by setting up changes in the metabolic processes of the tissues, and thus probably the production of some insufficiently broken-down excretory product, which in the course of circulation affects the peripheral nerves, causing symmetrical parenchymatous degeneration. The process may be compared to that in diabetes, in which the lack of the normal internal secretion of the cells in the islands of Langerhans in the pancreas so alters normal metabolism that an excess of dextrose is produced in the breaking down of the muscular tissue. Yet it is probably neither the dextrose in the blood, nor the acetone or diacetic acid by-products, which are the actual toxic agent in producing the neuritis. In diabetic neuritis there may be symmetrical numbness and anæsthesia of the extremities, with loss of deep reflexes, but little or no muscular paresis, though there is well marked ataxy, the so-called diabetic pseudo-tabes. In another form the pains may be extremely severe, and the muscular paralysis well marked, often in the distribution of one sciatic, external popliteal or anterior crural nerve. Why a circulating toxin should thus set up an asymmetrical neuritis is hard to understand; it is usual to explain it by inferring a locally acting cause in addition, such as overuse or strain of the limb, or undue pressure on the nerve. In the asymmetrical neuritis of rheumatism or of paratyphoid fever, the asymmetry may be due to local involvement of the nerve sheaths by direct organismal infection, as in leprous neuritis, but in diabetes no organisms are known to be at work.

Puerperal neuritis.—Polyneuritis developing shortly after childbirth, or even during the puerperium, is sometimes considered to be a septicæmic neuritis, due to sepsis acquired during parturition, or to retained septic products in the uterus from a previous pregnancy. I do not think that this explanation will cover all the cases of polyneuritis associated with pregnancy, but rather that some are true cases of autotoxæmia, the toxin which produces the polyneuritis being elaborated in the tissues as an abnormal by-product of the metabolism in pregnancy.

A year ago I had under my care for some months a young married woman aged 30, who ten weeks after childbirth complained of weakness of the legs and of numbness, and of pins-and-needles spreading in the feet and hands, followed by numbness of the abdomen and chest up to the neck. All the deep reflexes were lost, and she was unable to lift the legs off the bed; the extensors of the fingers also became weak, but the extensors of the thumbs and of the wrists were unaffected. Bilateral facial palsy and diplopia next appeared, followed by diaphragmatic palsy for several days.

There was deep tenderness of the calves and forearms, and well-marked anæsthesia of the feet and ankles, but she never suffered from any spontaneous pains. There was never any pyrexia or recognizable sepsis after the childbirth. She recovered completely after four months.

Ten years ago Batten [5] showed at a clinical meeting of this Society a woman with recurrent paralysis and wasting of the hands and legs, with absence of the deep reflexes, the paralysis recurring after two confinements. Such recurrent paralysis will be referred to presently as having been observed in other cases of apparently autotoxic polyneuritis.

Pressure neuritis as a cause of paralysis following childbirth must be carefully distinguished from toxic polyneuritis, the nerve that usually suffers being the sciatic, and especially its external popliteal portion, from pressure of the fœtal head upon it near its exit from the pelvis at the sciatic notch.

Cranial nerve paralyses are common as a sequel of ordinary pharyngeal diphtheria, the third, fourth and sixth nerves being commonly affected, and occasionally the seventh, fifth, tenth and twelfth. The loss of accommodation due to paresis of the ciliary muscle, that is such an early sign in post-diphtheritic palsy, I have also seen in septicæmic neuritis and in one other case of toxic polyneuritis. Walshe [43] has pointed out that the frequency of incidence of cranial nerve paralyses after diphtheria is dependent on the close contiguity of the source of the toxin in the pharynx, as, in cases of polyneuritis following accidental diphtheritic infection of an open wound of the trunk or limbs, cranial nerve paralyses are uncommon.

A definite syndrome has been claimed for *polyneuritis cranialis*, many observations being recorded of neuritis limited to several cranial nerves. Oppenheim [28] thinks these cases are usually due to a basal process involving the cranial nerves. Kinnier Wilson [44] showed at the Clinical Section a man who, after right-sided otitis media of three weeks duration, developed nerve deafness, of the right ear, right facial palsy, paralysis of the right half of the soft palate and of the right vocal cord, glosso-pharyngeal anæsthesia and hemiatrophy of the right half of the tongue, with bilateral loss of taste.

Slow chronic polyneuritis is a term that may be applied to cases in which the symptoms gradually increase during many months. Pain is usually either absent throughout, or only trifling at the commencement, but the muscular paralysis becomes extreme, and there may be extensive atrophy.

In the case of a man, aged 31, the symptoms gradually increased during twelve months, commencing with pain in the calves and a tired feeling, after the appearance of some large purpuric blotches on the legs.

The legs gradually became enfeebled to the stage of total flaccid palsy, the hands and forearms not being involved until nine months after the commencement of symptoms. When I saw him seventeen months after the onset, there was practically complete palsy of the feet and legs, hands and wrists, with contracture of the feet and hands. All the deep reflexes were lost and there was considerable anæsthesia in the periphery of all four limbs. The sphincters were normal, and no cause suggestive of polyneuritis could be discovered. Wassermann test negative in both blood and cerebrospinal fluid.

A girl, aged 15, became gradually weaker during twelve months until all four limbs were totally paralysed: she could not raise the head from the pillow, the eyelids and lips were partially paralysed, there was weakness of the masticatory muscles, and the tongue was somewhat wasted No sensory symptoms were present at any time except slight paræsthesiæ of the fingers at the commencement. All the deep reflexes were lost, but only slight muscular wasting occurred, and no contractures. No improvement was observable in spite of daily massage and electrical treatment until eighteen months after the onset, when she slowly began to regain power, and ultimately recovered perfectly in another two years.

The slow development of the symptoms in such cases strongly suggests a continuously acting toxin, rather than an acute poisoning, and one is driven to the supposition that an autotoxæmia is at work. In the girl's case at least the continual absorption of external toxins could be excluded, as her first symptoms occurred when at school in South Africa and advanced for three months at home some distance away, and she continued to get weaker for another nine months after being sent to England.

Relapsing and recurrent polyneuritis.—The commonest causes of recurrent polyneuritis are chronic alcoholism and lead poisoning, but recurrence is also met with in cases where the cause is obscure. F. G. Thomson [42] recorded the case of a youth of 19 in whom weakness commenced in the hands and feet five days after being thrown out of a sculling boat; within another ten days there was complete paralysis of all four limbs and of both sides of the face, with considerable weakness of the trunk muscles. The sensory symptoms were confined to slight numbness of the fingers and the soles of the feet. All the deep reflexes were lost and considerable wasting developed later in the muscles about the shoulders, forearms and legs, the extensors being chiefly affected. Recovery was complete in every respect in about two years. An interesting fact in the history was that this boy at the age of 5 years had had apparently a similar attack of motor paralysis affecting all four limbs, ending in complete recovery in eighteen months. The acuteness of the onset of the paralysis following the immersion is strongly suggestive of chill being the exciting factor, though his previous similar attack at the age of 5 seems to demonstrate a predisposition in his metabolic processes to the development of a neurotoxin, or possibly an excessive sensitiveness of his peripheral nerves to the action of such neurotoxin.

In lead poisoning it seems to be established that a recurrence of wrist-drop and colic may be dependent upon some slight cause, as a febrile attack or an irregularity in diet, in the total absence of any fresh source of lead absorption. This fact lends support to Mary Sherwood's suggestion [36], that the first attack of neuritis leaves the nerves with a lowered power of resistance to the assault of a fresh toxæmia.

Grocco [15] was the first to describe recurrent attacks of polyneuritis in the absence of any obvious cause such as lead or alcohol. Other reports of such cases have been made by Eichhorst [11], by Mary Sherwood [36], who described two cases from Eichhorst's clinic in Zurich, though her first case was that of recurrent palsy of the right arm only, and should scarcely be classed with other cases of generalized multiple neuritis. Ross and Bury [33] describe two sisters with recurring paralysis. Targowla [40] recounts the case of a woman who had three attacks of paralysis at the ages of 19, 27, and 39 years. Sorgo [37] described the case of a man who after three attacks of abdominal pain and constipation developed bilateral palsy of the arms, followed twelve months later by a recurrence of the paralysis and colic, and again eight months later following a chill, colic, severe pains, paralysis of the arms, weakness of the legs, loss of the knee-jerks, respiratory paralysis and death. Degenerative neuritis was found in the peripheral nerves. The sequence of the paralysis to attacks of severe abdominal pains and constipation is suggestive of an enterotoxin having been the cause, and is strikingly similar to the mode of onset of the paralysis in acute hæmatoporphyrinuric polyneuritis.

H. M. Thomas [41] published a clinical lecture on Recurrent Polyneuritis, describing the case of a man of 28, who had five attacks of paralysis within six years. In his case chronic indigestion was a feature of the illness, and possibly here also an enterotoxin was the cause.

A somewhat similar case was published by Nattrass [27]; a boy aged 18 developed double foot-drop, loss of deep reflexes, and other signs of generalized multiple neuritis, who had had two similar attacks of paralysis lasting for several months, one at the age of 4 and the other at 17. A pecularity in his case was enlargement and tenderness of the nerve trunks, especially of the median, ulnar and external popliteal.

Hæmatoporphyrinuric polyneuritis.—In 1908 my attention was first drawn to this curious syndrome :—

A woman, aged 47, was admitted to St. Mary's Hospital with pains in the abdomen, following a cold three weeks previously. Her pulse was 120, and the urine was noticed to be dark reddish coloured, hæmatoporphyrinuria being found on analysis. A week later she began to complain of pains all over her limbs and body, and it was found that she could not raise her arms to the level of the shoulder. The pains were worst in the arms and shoulders, but there was no anæsthesia. In five days she was unable to sit up or to feed herself. Insomnia became troublesome, and there was retention of urine, with overflow incontinence. The pains in her arms were so severe that she complained of feeling as if the skin was being torn off. The knee-jerks were present on admission, but were afterwards lost for some weeks. Three months later she could just hold out her arms, but there was still complete paralysis of the extensors of the fingers on both sides, with reaction of degeneration, though the extensors of the wrist and supinator longus were unaffected. Ultimately she recovered completely, the hæmatoporphyrinuria having disappeared before she left hospital.

It was not until February 1921 that I met with another case of this disease.

A man, aged 45, well nourished and living in perfect conditions in the country, apparently in perfect health except that he had always been obstinately constipated, was seized with pains in the back. Next day his urine was dark red coloured. The pulse was 60, and he now complained of severe pains around the loins and the front of the abdomen, at first thought by his doctor to be renal colic and then an acute abdomen, for which he was sent into a nursing home and a surgeon fetched from London. The latter however, refused to operate, making a diagnosis of acute pancreatitis. All the next week his pains were severe, and he was said to be jaundiced, and to have bile in the urine. On the fourth day there was retention of urine requiring use of the catheter. After eleven days he became excitable and nervous, owing to which I was asked to see him. The pulse was then 100, the strength of limbs and trunk good, and he could stand and walk. The knee-jerks were normal, as were all the other reflexes. He complained of some paræsthesiæ of the trunk, and, taken with his excitable nervous condition and sleeplessness, I thought he was developing acute mania. There was no history of venereal disease and his cerebrospinal fluid was normal. Two days later I saw him again; he could still stand, but the knee-jerks were now absent, and there was no weakness or anæsthesia. He again had retention of urine, and on the doctor passing the catheter I was astonished to see that the so-called bile-stained urine was port wine coloured, an extreme example of hæmatoporphyrinuria. Three days later he complained of "deadness" of the chest and abdomen when touched, and large areas in this region were found to be analgesic. Paresis of the deltoids was now well marked, as well as weakness of the flexors of the hips, but no other weakness of the limbs. His rectal temperature was now for the first time slightly raised; two days later his temperature was 100° F. and the pulse 132. He was now much weaker, unable to turn in bed and to cough owing to weakness of the abdominal muscles. The constipation became more and more extreme, the diaphragm paralysed, and he died after an illness of three weeks' duration. Unfortunately an autopsy was not permitted.

Needless to say, in both these cases sulphonal and other drugs as a possible source of poisoning were excluded. In both acute abdominal pains were amongst the earliest symptoms, followed immediately by hæmatoporphyrinuria, pains all over, paræsthesiæ and paralysis, especially of the arms, loss of knee-jerks, retention of urine and insomnia. In neither of my two cases was vomiting noted.

Hæmatoporphyrinuria may occur with symptoms of acute illness quite unconnected with the taking of any drug; it was first described in a case of acute rheumatism by MacMunn in 1880 [26], under the name of urohæmatin.

Acute attacks are ushered in by severe pains in the abdomen and loins, constipation, and sometimes vomiting. Dark-brown to port-wine coloured urine is an early symptom, and the pains continue and may spread all over the trunk and limbs. The pulse-rate is raised to 100 or 120, but usually there is no pyrexia. Retention of urine and even incontinence may occur, and occasionally mental symptoms may be noticeable, such as general nervousness, excitability, or even delirium and epileptic fits.

Gunther's excellent article [17] quotes fourteen cases in the literature, in four of which severe paralysis rapidly developed, followed by death soon after the onset of the paralysis, the earliest recorded case being that of Ranking and Pardington in 1890 [31].

These observers described the cases of two single women aged 41 and 47, both living in the same house, who were both taken ill with hæmatoporphyrinuria within a week; both were extremely neurotic, dyspeptic and constipated.

In the first case the symptoms followed immediately after a large dose (20 gr.) of acetanilide had been given in three doses within four hours. Partial suppression and retention of urine, which was port-wine in colour, followed immediately, and death occurred a week later, the legs being paralysed for a day before death. Their second case developed no paralysis and recovered, though the symptoms otherwise were similar. It is difficult to believe the possibility of simple coincidence for such a rare condition as hæmatoporphyrinuria in these two cases, in the absence of some common factor, as a drug, of which however there is no record, except the excessive dose of acetanilide in the first case.

Schulte [34 described the case of a ship's cook, aged 35, who was seized with abdominal pains, hæmatoporphyrinuria, followed by typical multiple neuritis affecting the arms only, paresis of the deltoids, biceps, supinator longus, infraspinatus and the extensors in the forearms. The pulse was only 48, there was no pyrexia and the man recovered.

Bachlechner [2] has recorded a case of hæmatoporphyrinuria followed by symmetrical wrist-drop and foot-drop, with the reaction of degeneration, in which the paresis developed with two succeeding attacks of the acute symptoms; and Gunther [18] states that repeated attacks of the syndrome of acute hæmatoporphyrinuria may occur within a year, though in none of his own cases did polyneuritis develop.

L. F. Barker and Estes [3] observed a girl aged 18 with hæmatoporphyrinuria and polyneuritis which ended fatally after sixteen months. She passed dark urine for the whole of that time, and suffered from pain in the lower abdomen, recurring nausea and vomiting, vertigo and epileptic fits. Laparotomy disclosed a dilated pylorus and duodenum. Two months later, after complaining of severe pains all over, bilateral wrist and foot drop developed, with extensive muscular atrophy, including the intrinsic hand muscles. The deep reflexes were at first exaggerated but later lost, and she died four months later. At the autopsy there was found great distension of the stomach and duodenum. A very interesting point in this case was that the family history disclosed the fact that four other members of the family seemed to have suffered similarly with hæmatoporphyrinuria and nausea with abdominal pains, one of her sisters having died after being ill for nine months with similar symptoms. The strong family tendency to these symptoms, associated with hæmatoporphyrinuria, is practically conclusive evidence of an autotoxæmia being the origin of the syndrome. In all probability an intestinal toxin is to blame. Barker and Estes regard the gastro-duodenal dilatation as primary, the toxæmia producing the hæmatoporphyrinuria and polyneuritis being secondary. In my second and fatal case the obstinate constipation was a striking and troublesome symptom from which he had always suffered, and it is suggestive that the toxæmia was intestinal in origin.

Gunther applied the term acute toxic hæmatoporphyrinuria to those cases in which the symptoms follow chronic poisoning by sulphonal, trional, tetronal, veronal or its derivatives. Lead, saffron and glycerine, are also said to produce toxic hæmatoporphyrinuria.

Hæmatoporphyrinuria resulting from the use of sulphonal was first observed by Stokvis [39], in the case of a woman who passed port-wine coloured urine after taking sulphonal for many months. Schulz [35] described a fatal case after taking 15 gr. of trional daily for one month, the symptoms being epigastric pain and vomiting, and followed by loss of strength two weeks later, hæmatoporphyrinuria appearing for a few days before death. Many cases of this acute sequel of chronic sulphonal or trional poisoning have since been published, and in about one-fourth of them acute paralysis has been noted. The syndrome closely resembles that of acute hæmatoporphyrinuria not due to drugs. Thus, severe abdominal pains, vomiting and constipation, are often prominent symptoms, recovery rarely happening when all these three symptoms are present. A typical case was described by Anson [1]. A woman, aged 35, after taking 30 gr. of sulphonal daily for three and a half years, developed acute abdominal symptoms, constipation, hæmatoporphyrinuria, intense pains in the legs, loss of knee-jerks, followed ten days later by marked weakness of the legs, increasing to total paralysis, the arms being later similarly affected. There was no anæsthesia, but incontinence of both sphincters until death. In this case no toxic symptoms appeared until the drug had been taken regularly for three and a half years, but in other cases the symptoms have come on acutely after even one or two doses of trional or sulphonal.

In Keith Campbell's case in 1897 [7], in the Royal Asylum, Perth, a domestic servant, aged 22, nervous and depressed, and suffering from constipation, was given two powders of 15 gr. each of sulphonal and phenacetin. Vomiting commenced four days later, and hæmatoporphyrinuria fourteen days after taking the drugs. Convulsions developed as well as nystagmus, progressive paralysis, loss of the knee-jerks, and death occurred thirteen days after the first vomiting.

Stockton [38] described a case of acute ascending paralysis with hæmatoporphyrinuria in a girl, aged 27, who, previously strong and healthy, became obstinately constipated, and twelve months later nervous, irritable and anæmic. She was given three doses of 5 gr. each of sodium salicylate and sulphonal. Vomiting set in, the pulse became slow and the urine claret coloured. Fifteen gr. of sulphonal was given and next night a similar dose of trional, but both failed to induce sleep. Anæsthesia of the buttocks appeared, followed by incontinence of both sphincters, shooting pains in the legs, progressive paralysis and anæsthesia, the arms being last affected, and loss of the knee-jerks. Some power returned in the feet and legs but the arms remained totally paralysed, and there was total loss of sensation on the trunk and lower limbs. Doubtful optic neuritis was observed before death. No autopsy was obtained. In the discussion on this paper, Putnam [30] referred to a case of his own of increasing paralysis with hæmatoporphyrinuria following the administration of sulphonal, in which degenerative neuritis was discovered at the autopsy, the spinal cord being normal.

A case of hæmatoporphyrinuric polyneuritis following the use of trional was published in 1901 by Hart [20], in which recovery occurred. Trional differs from sulphonal only in the substitution of an ethyl group, C_2H_5, for a methyl group, CH_3. His patient was a woman, aged 50, who had taken much trional for a long time, when acute colicky abdominal pain with nausea and vomiting developed. There was no pyrexia, abdominal tenderness or distension. Five days later hæmatoporphyrinuria appeared, followed within a week by progressive paralysis of the extensors of the feet and wrists, with severe pains, anæsthesia and loss of deep reflexes. There was delirium and psychosis of Korsakow type. The pains in the limbs and abdomen were excruciating for a time, and limb contractures developed, followed by a slow recovery.

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ON MUSCLE TONUS.

DE BOER'S EXPERIMENT ON THE FROG.

(From the Physiological Laboratory, Utrecht.)

BY J. W. LANGELAAN.

DE BOER'S experiment consists in cutting the rami communicantes which unite the sympathetic chain with the spinal nerves of the lumbar plexus. After their section the frog is fixed in a clamp by means of a hook through the nose, as was first done by Brondgeest. When hanging in this way the difference in position and in length of the two hind legs can be observed. In these experiments the frog was always intact, that is the spinal cord was not divided. According to de Boer the leg on the side on which the rami communicantes are cut is invariably more extended and slightly longer than that of the normal side, and he attributes this difference to a loss of tonus of the muscles of this limb. He states that the loss of tonus in this case is as complete as after the section of the posterior roots of the lumbar plexus. This effect, according to de Boer, is permanent, and he concludes that muscle tonus is governed exclusively by the sympathetic system, and that the impulses maintaining tonus reach the muscles by way of the rami communicantes.

The same experiment repeated on the cat has yielded similar results. The definition which de Boer gives of tonus is the same as that of Johannes Müller, Brondgeest, and the great majority of recent investigators, viz., a state of slight contraction of muscle.

In repeating this experiment I performed the operation as carefully as possible. The frog was rendered motionless by being wrapped in cotton wool and the needles which fixed the animal pierced the wool only. The intestines were always kept within the abdominal cavity and pushed aside by means of a little tampon moistened in Ringer's solution. The blood-vessels were spared as far as possible, especially the large vena dorso-lumbalis (Gaupp). Before reaching the rami communicantes, the parietal peritoneum must be incised and in most cases the kidney pushed a little aside. In this latter manipulation, as well as during the section of the rami communicantes, it is difficult to avoid stretching the sympathetic chain and its branches. The stretching of these nerves increases and lengthens the period of shock following the section of the rami.[1] The same effect is produced by bringing the intestines outside the body in order to facilitate the operation; most observers have done so and consequently produced severe and prolonged shock of the spinal reflex arcs.

I have performed the operation in every case on the right side only upon male frogs of moderate size. The operation is much more difficult in *rana temporaria* than in *rana esculenta*, and in many other respects too the former is not so suitable for the experiment. I usually divided the rami communicantes uniting the sympathetic chain with the seventh, eighth and ninth spinal nerve trunks, but in some cases the sixth ramus was also sectioned, and in others the tenth.[2] The latter ramus is very slender and does not seem to influence the muscles of the hind limb. As the wound must be carefully sewn up, this part of the operation took approximately a quarter of an hour and consequently I never observed the animals earlier than ten to fifteen minutes after the section of the rami communicantes.

Rana esculenta survived the operation well for several weeks, after which the animals were then killed for the purpose of autopsy; *rana temporaria*, however, stood the operation badly, suffered from severe shock and often died within the course of a few days. I think this was chiefly due to the bad state in which the animals reached the laboratory during this year.

When a normal frog is suspended by means of a hook piercing its nose, its first act is a defensive movement. By placing its feet against the hook and then stretching its extremities with force, it tries to free itself from it. A small drop of a 3 per cent. solution of cocaine upon the wound through which the hook passes often suppresses these movements. As soon as the defensive movements cease flight movements appear. In *rana esculenta* swimming movements are more common, whilst in *rana temporaria* jumping movements prevail. In its natural state a frog performs two different kinds of swimming movements; ordinary swimming, that is symmetrical and synchronous movement of the four legs, and alternating swimming movements. As soon as the fore-part of the body meets an obstacle when swimming in the ordinary way the movements become alternate; then the extended right fore-limb is flexed and adducted to the chest, and the flexed and adducted left hind limb is extended with force. These movements alternate with the reverse movements of the contralateral limbs; they are slower and less strong than the symmetrical swimming movements. On reaching land this alternating movement insensibly develops into creeping. Alternate swimming is, therefore, the transition between swimming and creeping, or it is a creeping movement in water. The jumping movement is always symmetrical, consisting chiefly in a forced extension of both hind limbs. All these movements are slightly modified when the frog is suspended, but in general they are easily recognized.

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[1] The term "shock" is used for that temporary suppression or depression of nervous function which follows immediately upon mechanical injury of some part of the nervous system.

[2] The spinal nerve leaving the cord between the first and second vertebræ is reckoned as the first spinal nerve.

In my experiments the hook that pierced the nose was not attached immediately at the clamp, but was held by another hook fixed into the clamp. This arrangement allowed rotation to occur round the vertical axis as soon as the animal executed a movement which was not strictly symmetrical. Most observers using the suspension method of Brondgeest seem to have attached their animals in a similar way, so that there is scarcely any doubt that the reflexes caused by these rotations hampered their observations. The rotation movements which occur in my arrangement have in general a small amplitude and a quickly increasing and decreasing angular velocity. The frog is said to rotate clockwise when the rotation is in the same direction as the hands of a watch placed with the dial plate upwards; when the movement is reversed we say that the frog rotates anti-clockwise.

Such a rotation stimulates both labyrinths simultaneously but not to the same degree. Clockwise rotation stimulates chiefly the left labyrinth, anti-clockwise the right. The two labyrinths act synergically in the reflex movements they produce; these are most marked in the hind limbs, but they occur in the fore limbs too. The movements of the hind limbs are chiefly extension and flexion; the extension movement begins with spreading of the toes, combined with forced extension of toes and foot, followed by extension at the knee-joint and later by abduction of the whole leg from the middle line, combined with a slight ventral adduction at the hip-joint. The flexion movement commences with adduction of the toes, associated with flexion of toes and foot; then flexion at the knee-joint, followed by adduction of the whole leg towards the middle line, and a slight dorsal adduction at the hip-joint. The extension movement of the fore limb commences with a slight spreading of the fingers, followed by extension of the arm and abduction from the body. The flexion movement begins with a slight adduction of the fingers, associated with flexion of the arm and adduction of the whole limb against the chest. The reflex movements resulting from the rotation of the suspended animal are shown in the following synoptic table.

Animal rotating Anti-clockwise (Right Labyrinth chiefly stimulated).

Right labyrinth	Hind limb	Right, forced extension.
		Left, flexion.
	Fore limb	Right, extension.
		Left, flexion.
Left labyrinth	Hind limb	Right, extension, weak or absent.
		Left, slight flexion.
	Fore limb	Right, extension, weak or absent.
		Left, slight flexion.

When the animal rotates clockwise it is the left labyrinth which is chiefly stimulated, and the resulting reaction may be deduced from the table by interchanging right and left.

The movements elicited reflexly from the labyrinths are rather slow and are executed with considerable force. They commence in the toes and foot of the same side as the labyrinth which is stimulated by the rotation, so that when the animal turns clockwise it is the toes of the left foot which first spread. If the stimulus is weak, or the threshold high owing to the exhaustion of the reflex, the only obvious reaction is the spreading of the toes, the slight extension of the limb often escaping our attention.

The reflex elicited by the rotation of the suspended frog was first described and recorded photographically by Dusser de Barenne [7], who proved its labyrinthine origin. This reflex must not be confounded with the automatism provoked by suspending the frog by means of a twisted string, so that the animal turns slowly and always in the same direction. Like all reflexes in the suspended animal, the rotatory seems to be a normal reflex, for if we imagine the animal in its natural position with its four legs touching the ground the extension of the limbs of one side would check rotation round its cranio-caudal axis. According to the researches of Quick [16], this is the normal reflex movement elicited in all vertebrates by stimulation of the semicircular canals. The rotation reflex is therefore probably a normal labyrinthine reflex, slightly modified by the suspended position of the animal.

When the animal has been suspended for some time, the irritability of the semicircular canals is increased owing to the abnormal position, and consequently even a slight degree of rotation is followed by a reflex movement. It is not possible to eliminate the reflex by suspending the frog by a single hook, since rotation may still occur owing to the elastic nature of the tissues in which the hook is fixed; under these conditions the excursions are greatly diminished and easily escape our attention, and we may be therefore deceived by the reflex movements provoked by them.

When the intact frog is suspended the defence automatism is the predominant reaction, and when it is eliminated the rotary reflex usually prevails. As soon therefore as flight movements produce a slight rotation of the animal, they are suppressed by the rotation reflex. If the spinal cord of the frog is divided between the second and third spinal roots the defence and the rotatory reflexes are abolished, and the flight reflexes prevail. The swimming and jumping movements, however, have no longer the same precision as in the intact animal, and are often arrested before the apparent aim of the movement is attained; in other words, the automatism subsides into a simple sequence of spinal reflexes.

It has been pointed out that the difference in the position of the two hind limbs may be rendered more evident by immersing the frog in water. Water being a dense medium of approximately the same specific density as the tissues, the tensional stresses existing in the muscles have free play to develop their strains when the animal is immersed. But water, in consequence of its density, also restricts movements, which consequently either do not occur, or cease earlier than they would in air. But the reactions observed when the suspended frog is immersed may not be the normal ones, since the immersion may act as a physiological stimulus. If the frog is lowered slowly and at a uniform rate and no farther than the middle of its body, into water of exactly the same temperature as the room, the immersion seems to have no stimulating effect, but if these precautions are neglected swimming movements are often elicited. Immersion into water of much lower temperature than the room seems to increase the flexion of the hind legs, but not to influence extension. This method therefore introduces many sources of error and cannot be considered an improvement. The suspension of a normal frog by a hook is also an unsatisfactory method, and I should not have employed it if the question whether efferent sympathetic nerves influence the tonic state of the muscles had not been raised by de Boer's experiments performed by it.

In an earlier publication [10] I tried to show that muscle tonus depends upon two different properties of muscle, and that these two properties are governed by two different sets of efferent nerves. Shortly afterwards and independently, Pieron [14] [15] came to the same conclusion. The first property of the tonic muscle is plasticity. A body is said to be plastic if its form is permanently altered when a stress to which it is subjected is removed. It follows from this definition that if the body was in a state of equilibrium before the deformation, it will be again in equilibrium after the deformation. If, therefore, the form of a plastic muscle is altered for a moment by the action of internal or external forces, the deformation produced by these forces is partly permanent. The greater the permanent deformation in comparison with the total change of form, the more plastic the muscle. Hence, if a muscle contracts a shortening remains, while if it is extended by the action of its antagonists a lengthening is the result; whereas a muscle which has lost its plasticity returns after each change of form to the same definite length. It is evident that a permanent deformation in a muscle is not attended by a continued expenditure of energy nor accompanied by rhythmic electric phenomena, while the production of a permanent deformation, or a variation in an existing deformation, is accompanied by the expenditure of free energy and by electric phenomena[1]. Plasticity, I believe, is intimately connected with what is usually called the "trophic state" of the muscle, and the degree of plasticity may possibly therefore prove to be a measure of the trophic state of muscular tissue.

Plastic tonus is that state of the muscle in which it has the properties of a plastic body. This term is chosen to indicate that the plasticity of muscle is maintained and controlled by the central nervous system. As shown in an earlier publication [7], an isolated muscle may be deprived of its plasticity by physical disturbances of the same kind as occur during the normal function of the muscle. There is, therefore, no doubt that the maintenance of plasticity is a function of the central nervous system. Hence, plastic tonus is a reflex tonus. It shows itself not so much during movement as after movement. It influences therefore the attitude of the animal, and its diminution or loss must alter normal postures. Sherrington, especially [17] in his article on reflex postural activity, called attention to this function of the tonic muscle. During movements plastic tonus influences the steadiness of the movement, and its diminution or loss is revealed by unsteadiness of movement.

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[1] Electric phenomena have been observed by de Meyer [12] in non-permanent deformation of muscle.

The second property of the tonic muscle is the faculty of maintaining a state of slight contraction. This property of muscle I proposed to call *contractile tonus.* It is the reflex tonus of Johannes Müller, Brondgeest, de Boer and of most of modern authors; it is now generally admitted that it is maintained and controlled by the central nervous system. When in a state of contractile tonus the muscle is not in equilibrium, but in a state of slight contraction. For this reason the maintenance of the contractile tonus is accompanied by the expenditure of free energy and by rhythmic electric phenomena; and it is therefore intimately connected with heat production, especially in the homoiothermic animals. The view that reflex tonus comprises two components is in harmony with recent morphological researches of Boeke [1], as well as with the researches of Wertheim Salomonson [18] on the electric phenomena of tonic muscle.

In order to avoid confusion, I will use the word "tonus" as the general term, comprising the two components, plastic and contractile tonus. The part played by each of the two components in the joint results is left indeterminate. The terms "plastic tonus" and "contractile tonus" will always be used strictly in the sense defined above.

The first group of experiments was made on intact frogs, the spinal cord not being cut. The seventh, eighth and ninth rami communicantes were divided on the right side. As soon as the animal is released, a quarter of an hour after the operation, it immediately regains its natural position and jumps away; when placed in the basin it swims. The voluntary movements seem almost normal, but the animal, when jumping or swimming, often deviates a little from the straight line. On squatting immediately after having made a jump, the attitude is abnormal (fig. 1). The trunk deviates to the left, the right hind limb is abducted from the body, the knee points laterally and the foot is not covered by the leg; the area of the limb in contact with the ground is larger than on the normal side. It is evident, on examining the mid-dorsal line, that the superior part of the trunk forms an obtuse angle with the inferior part. Below the level of this angle on the right side the papillæ of the skin are flattened and the skin itself is darker. On the photograph reproduced in fig. 1, these changes, characteristic of loss of function of the sympathetic system, are very striking upon the trunk, but they exist also, though less distinctly, upon the right hind limb. When the animal sits quietly the curvature of the trunk gradually diminishes in the course of some minutes, but a slight deviation remains. The abnormal position of the hind limb is usually also corrected, but as this correction takes place abruptly it gives the impression of volitional movement. The slight deviation of the trunk at rest persists for a period of four to six weeks, and then disappears in consequence of gradual compensation, which may go so far as to lead to slight deviation of the trunk to the opposite side. As I will show later, it is impulses emanating from the left labyrinth which bring about this compensation. As soon as the frog comes to rest and floats upon the water after swimming, the right hind leg is not adduced to the body, but remains partly extended and hangs down (fig. 2). Sometimes extension is the most striking feature, at other times it is drooping of the leg. In consequence of this abnormal attitude, the frog no longer floats symmetrically, but the right half of the body, and especially its posterior part, is more submerged. When floating quietly this abnormal position may persist for a long while, but it is usually

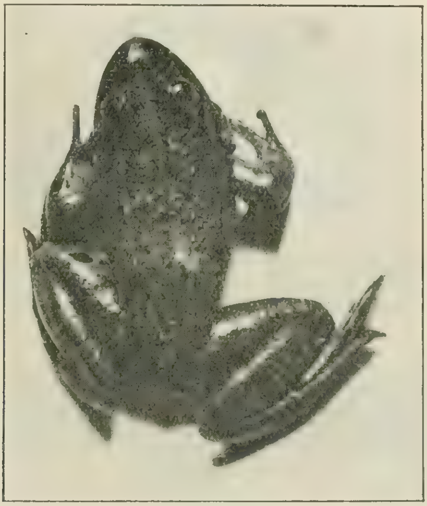

FIG. 1.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side; photograph on the following day to show the attitude of the animal three minutes after having made a jump.

corrected, apparently volitionally, in the course of some minutes. The abnormal attitude of the hind limb is permanent and may be observed for several weeks after the operation (fig. 3); complete compensation did not occur in the course of my experiments. These different abnormal postures are easily observed in *rana esculenta;* in *rana temporaria* they are often absent shortly after the

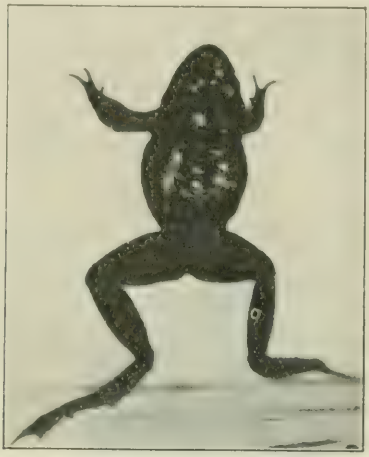

FIG. 2.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on December 27, 1921. Photographed next day as the animal floated on water. The right side of the body is more deeply submerged, and the right hind limb hangs down.

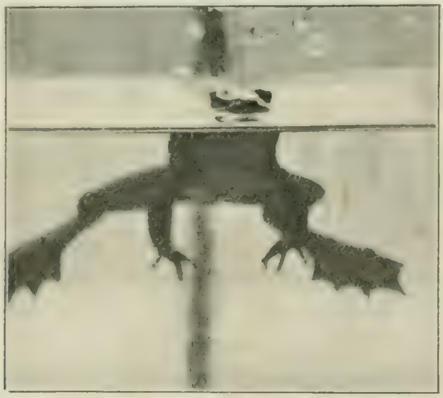

FIG. 3.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on January 4, 1922. Photographed on January 28, 1922, as the frog floated in water; front view. The right half of the body is more deeply submerged, and the right hind limb is more extended and hangs lower. Same animal as in fig. 4.

operation in consequence of local shock, and later they are mostly obscured by the restlessness and lively movements of these animals.

When the frog is suspended immediately after the operation[1] the right hind limb is extremely flabby, more extended and slightly longer than the normal one. The flabbiness of the limb is the most striking phenomenon and is always present. It may be demonstrated by quickly moving the frog to and fro; then the right limb swings more easily, the amplitude of its movement is larger and it continues to swing after the normal limb has come to rest. If jerked up and down its movements are irregular, whereas the normal limb moves more smoothly. The flabbiness of the musculature is also shown by the form of the leg (fig. 5). The calf is flattened and the pretibial muscles hang down along the bone so that their greatest prominence is slightly lower than on the normal side. Similar differences may be observed between the two thighs. The flabbiness of the hind limb gradually diminishes in the course of the first day after the operation, but then remains approximately unchanged for at least two months. What happens after this period I do not know.

On comparing the attitudes of the hind limbs when the frog is suspended during the first hour after operation, it is evident that the right limb is more extended and that the right foot droops. The increase in the length of the limb is chiefly due to this abnormal position of the foot. When measured by means of a horizontal microscope it amounts to approximately 3 to 4 mm. in a middle-sized frog of about 185 mm. in length from nose to toe. In some cases the difference may reach 5 mm. immediately after the operation. If the animal is then carefully immersed in water the difference in the position of the legs becomes more obvious, and the flabbiness of the limb is more evident, for even the slightest vibration of the fluid is communicated to it, whilst the normal leg remains at rest. Some time after the operation the difference in position and in length of the two legs begins to diminish. If the operation was performed carefully recovery sets in within an hour, but if done roughly it may persist several hours. At the end of the first day, a state is usually reached which seems stationary for several days, till compensation becomes perceptible. In this stage, the difference in length between the two legs amounts to 1·5 to 2·5 mm. when the animal is hanging quietly.

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[1] The descending root of the nervus trigeminus reaches the lumbar region of the cord in the frog. If, therefore, the hook piercing the nose deviates a little from the middle line, e.g., to the right, flexion reflexes may be evoked in the right hind limb by stimuli emanating directly from the wound made by the hook.

In experiments in which the operation happened to be easy and stretching the sympathetic chain and the rami communicantes could be avoided, I observed that immediately after the operation the right limb was more flexed and shorter than the normal one, but in the course of the first hour it became slightly more extended and longer than the left as the animal was hanging quietly. In these cases the final elongation never exceeded 2·5 mm. I am inclined to believe that in this instance the local shock was very slight, and that the section of the rami communicantes may have acted as a stimulus.

As soon as the frog is suspended immediately after the operation it usually makes defence movements. When this reaction to its abnormal position has ceased spontaneously or is suppressed by a drop of cocaine solution, the rotatory reflexes and those elicited from the skin are either abolished or strongly diminished on the right, and often slightly depressed on the normal side too, in consequence of the local shock produced by the section of the rami communicantes. The degree of depression of the reflexes depends chiefly upon the manner in which the operation was performed ; if easy the depression is slight and of short duration ; if, on the other hand, difficult and attended by stretching of the sympathetic chain, the depression is deep and prolonged. The first reflex that can be elicited is always the rotatory reflex. It reappears during the first hour after the operation and long before the stationary state is reached, in which the elongation of the right hind limb amounts to no more than 1·5 to 2·5 mm. It is evident, as the local shock is disappearing, that the reflex movements provoked by the stimulation of the right labyrinth are diminished, so that the movements evoked from the left labyrinth become preponderant. The depression of the function of the labyrinth on the side on which the rami communicantes are cut remains permanent during the whole period of observation, and one gets even the impression that the predominance of the left labyrinth increases rather than decreases. A glance at the table on p. 437 will make it clear that the predominance of the left labyrinth causes extension to prevail in the left hind limb and flexion in the right hind limb (fig 4). Moreover, the abnormal position of the animal increases the irritability of the labyrinths, so that even the slightest and hardly perceptible rotation provokes a reflex movement. As a result of the manner in which the animal is suspended there is probably no active movement which is not accompanied by a rotatory component, and the labyrinths are therefore incessantly stimulated. The rotatory reflex, as already said, is strongly dominant, and therefore after each active movement of the animal the right limb is temporarily shortened and the left limb temporarily extended. This is the reason why Dusser de Barenne [6] observed shortly after the operation that the hind limb on the side on which the rami communicantes are severed is shorter than that on the normal side. It is only during the period of local shock, when the rotatory reflex cannot be elicited, or at the moments when the labyrinthine reflexes are exhausted, or, finally, when the animal has been hanging quietly for at least a quarter of an hour, that the elongation following section of the rami communicantes can be observed in the frog in which the spinal cord is intact. I have also tried to demonstrate the difference in function between the two labyrinths by placing the frog upon a rotating disk. The correction movements, however, are chiefly executed by the head and those parts of the trunk lying above the level where the rami are divided. The method afforded, therefore, no definite results.

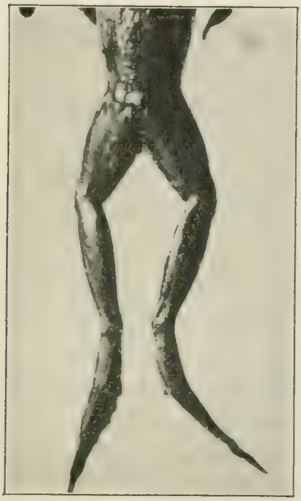

FIG. 4.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on January 4, 1922; photographed January 25, 1922. The flexion of the right hind limb when suspended is due to predominance of the left labyrinth. The same animal is shown in fig. 3.

The reflexes that return next are those elicited from the skin. The first to appear is the simple flexion reflex, quickly followed by swimming movements, especially in *rana esculenta*, and by jumping movements in *rana temporaria*. The swimming and jumping movements often appear quasi-spontaneous. From the first moment that all these reflexes reappear, it is evident that the movements of the right limb lack steadiness; they resemble in this respect the movements in locomotor ataxia. This unsteadiness is a consequence of the diminution of the plasticity of the muscles, and may be observed for at least several days after the operation. For the same reason the deformation of the muscle after a contraction or after stretching is diminished on the right as compared with the normal side. The right hind limb, having executed a movement, returns, therefore, more nearly to its inherent equilibrium length than the normal one. It follows from these considerations that the difference in length of the two hind limbs, as soon as the local shock has passed away, is not a fixed quantity, but depends chiefly upon what happened just before the limbs were at rest. Owing to the predominance of the rotatory reflex the right hind limb is more likely to be shorter at a moment arbitrarily chosen than the normal one. This fact was actually observed in the frog by Yas Kuno [9] and by Negrin y Lopez in cooperation with von Brucke [10], in the cat. It was erroneously considered by these observers as being in contradiction with de Boer's observations.

Summarizing the result of this group of experiments, we conclude: *Section of the seventh, eighth, and ninth rami communicantes in the frog is followed by local shock of the primary reflex arcs of the spinal cord. During the period of shock, the loss of tonus is complete (de Boer [2]). As soon as the shock has passed off the loss of tonus is only partial (Dusser de Barenne [6]). As a result of section of the rami communicantes, the muscles lose a great deal of their plasticity. The diminution of the plasticity of the muscles shows itself most distinctly in the attitudes of the animal, but the movements also lack steadiness. The results of diminution of plasticity are gradually compensated by stimuli emanating from the labyrinths, especially from the labyrinth opposite the side on which the rami communicantes are divided.*

The second group of experiments was also made on intact frogs. In this group, the seventh, eighth, and ninth posterior roots were divided on the right side. As soon as the animal is released, approximately a quarter of an hour after the section of the roots, it regains its natural position. The attitude of the animal is normal, with the exception that the right hind leg is flabby and trails behind the body in consequence of local shock produced by the section of the roots. In the course of the first half-hour after the operation the leg begins to flex slightly and to adduct a little to the body. When in this period of recovery the animal floats upon the water in a basin, the hind limb is flexed, and brought almost into its normal position. At the end of the first day the right hind limb is still a little flabby. When the animal is squatting, the hind limb, in consequence of this flabbiness, projects a little from the body, and a greater surface of the leg touches the ground than on the normal side. Owing to the same reason the right heel is lower than the left. Sometimes the leg is more flexed than normal at the knee and the ankle joints, especially when the animal sits after having made a jump. This deviation from the normal position occurs only after the movement described by Hering [8] as the "tilt phenomenon." If the operation has been successful and local shock slight, the state of the animal immediately after it is approximately the same as it usually is at the end of the first hour.

When the animal is suspended directly the operation is terminated, the position of the right hind limb, as de Boer has stated, is exactly the same as it is after section of the rami communicantes. The difference in length between the two legs amounts at most to 5 mm. in a frog of normal size. This agreement in position and in elongation is due to the fact that in both instances the operation produces a severe local shock of the primary reflex arcs of the spinal cord, in consequence of which there is temporarily a complete loss of tonus. In the course of the first day after the operation, the difference in the position and length of the two legs diminishes, and finally the length of the right hind limb does not exceed the length of the normal one by more than 1 to 2 mm. This difference is still present a week after the operation. The rotatory reflex reappears within the first half-hour. At first the flexion and the extension of the right limb are somewhat feeble, but soon the difference between the reflex movements of the two sides is hardly perceptible. When the operation has produced but little shock, the rotatory reflex may be present from the first moment, and movement is almost normal—the only difference between the two sides being a slight diminution of the steadiness of the movement of the right limb. This unsteadiness is only perceptible during that phase of the reflex movement in which the foot is extended and the toes spread. When the animal has been suspended for a time even the slightest rotation provokes a reflex movement. This proves that the labyrinths become more irritable owing to the abnormal position of the animal.

Summarizing the results of this second group of experiments, we may conclude: *Section of the seventh, eighth, and ninth posterior roots in the frog is followed by local shock of the primary reflex arcs of the spinal cord. During the period of shock the loss of tonus is complete, as Brondgeest has stated* [4]. *As soon as the shock has passed off, a diminution of tonus remains. The postures and movements of the animal are approximately normal, so that the diminution of tonus seems chiefly, though not exclusively, due to a decrease of contractile tonus. The rotatory reflex is not permanently influenced by section of the posterior roots.*

The third group of experiments was made on frogs in which the spinal cord had been divided between the second and third spinal roots. When the animal is released, approximately ten minutes after the section of the cord, it usually regains its squatting position when put upon the table in the proper manner. Its posture, however, is more crouching than it was before. Recovery from shock begins in the course of the first day after the section, and then the reflexes gradually reappear. When the animal is suspended, the loss of tonus produced by the shock is complete in the distal part of the body; the hind limbs are flabby and the heels often touch each other. As soon as recovery sets in the tonus returns, at first in the more proximal parts of the limb, later in the foot and the toes. The reflexes that may now be elicited are the flexion and swimming reflexes. The irritability of the preparation increases as the shock passes off, so that the slightest touch of the skin, or even an insignificant jar, elicits a reflex. Flexion movements now prevail, since the extension reflex emanating from the labyrinth is abolished. In consequence of the predominance of the flexion movements the permanent deformation of the muscles is in the same direction, and so the well-known flexion contractures develop.

When the shock following the section of the spinal cord has largely subsided, approximately twenty-four hours after the operation, the seventh, eighth and ninth rami communicantes are divided on the right side. The local shock following the section is usually not so severe as when the cord is intact. The phenomena which may be observed in the suspended animal are qualitatively the same as when the cord is intact. When tonus returns the right hind limb remains flabby and is slightly longer than the normal (fig. 5). The difference in length, however, never exceeds 1 to 1·5 mm., and usually amounts to 1 mm. only. As this slight difference in length is not very obvious, it is the flabbiness of the hind limb and the unsteadiness of its movements which more clearly reveal the diminution of plasticity. The flabbiness of the limb, though diminished, still exists on the tenth day after the operation; I did not observe the animals for a longer period. The unsteadiness may be demonstrated by gently squeezing the two feet simultaneously; then the hind legs are raised and adducted to the body as if the frog were sitting, but the right limb is not so much adducted as the left, and falls abruptly when giving up this position. The left hind limb maintains the position somewhat longer and then falls slowly, often by steps. When the right leg is actively extended the movement is also abrupt, and the leg often passes for a moment its position of equilibrium. On stimulating the two feet simultaneously, I often got the impression that the right limb, the rami communicantes to which were divided, was not so irritable as the other. I sometimes observed a slight, hardly perceptible flexion of the left leg occurring to all appearances spontaneously; and while in this flexed position, which may be maintained for several minutes, the reflex irritability of

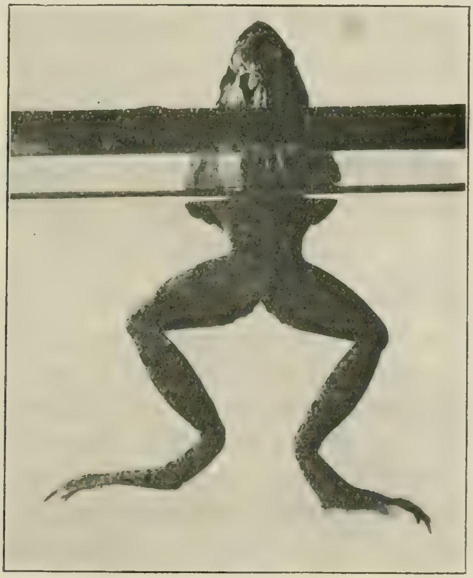

FIG. 5.—The spinal cord was transected 1·5 mm. below the calamus scriptorius on January 9 at 1 p.m. At 1.30 p.m. division of the sixth, seventh, eighth, ninth and tenth rami communicantes on the right side. Photographed at 1.30 p.m. on the following day to show the difference in position and length of the hind limbs when the animal was partly immersed in water. The right limb—and especially its distal part—is surrounded by a halo, owing to slight vibration transmitted to this limb from the water; it affected this limb only.

the leg was considerably increased, so that even touching the foot with the point of a fine human hair provoked a vigorous flexion reflex. I have the impression that this slight flexion of the leg is the same phenomenon as the shortening of the muscle which always precedes a muscle clonus [11]. In both instances, I believe, the shortening is due to impulses reaching the muscle from the sympathetic system. In several experiments the succession and the interval of time between the two operations was varied, but the chief results were always the same.

Summarizing the results of the third group of experiments, we may conclude : *Section of the spinal cord between the second and third spinal roots is always followed by severe shock in the distal part of the body. During the period of shock the loss of tonus is complete, and when the shock has passed, a diminution of the tonus remains. Subsequent section of the seventh, eighth and ninth rami communicantes produces a diminution of the plasticity of the muscles of the hind limb. After the section of the spinal cord, the rotatory reflex is abolished.*

The fourth group of experiments was made on frogs in which the spinal cord was only partially cut through. The experiments in which the section of the spinal cord between the second and third spinal roots was proved by autopsy to be incomplete, taught that the rotatory reflex, though feeble, may still be elicited if the external part of the antero-lateral tract and the zona marginalis only are left intact. A certain number of fibres subserving the reflex reach, therefore, these regions of the spinal cord at the level not below the second spinal nerve.

In another set of experiments the more lateral region of the medulla oblongata, 1·5 mm. above the calamus scriptorius, was cut through on one side. The more medial region of the oblongata, containing the fasciculus longitudinalis posterior, was always spared. I divided therefore the formation known in the higher vertebrates as the corpus restiforme. The effect upon the posture of the animal resembles that produced by the section of the rami communicantes, but is much more pronounced and extends over the whole side of the body on which the corpus restiforme is divided, so that when swimming or jumping the animal deviates considerably from the straight line, and when squatting the whole body is curved to one side. The rotatory reflex emanating from the labyrinth on the side on which the corpus restiforme is injured is abolished.

Summarizing the results of this fourth group of experiments, we may conclude: *The fibres conducting tonic impulses from the labyrinth to the muscles pass by the way of the corpus restiforme; a certain part of the fibres subserving the rotatory reflex enters the tractus anterolateralis of the spinal cord.*

The results of this research have led to a scheme of the primary spinal reflex arcs which differs from the current conception. While I was completing this scheme, Bok [3] published his morphological researches on the structure of the spinal cord. The results at which we had arrived independently agreed so closely that we have tried together to plan a scheme of the primary reflex arcs of the cord. In fig. 6 this scheme is reproduced. We started with the idea that the primary spinal reflex arcs subserve, in the first place, the more primitive spinal

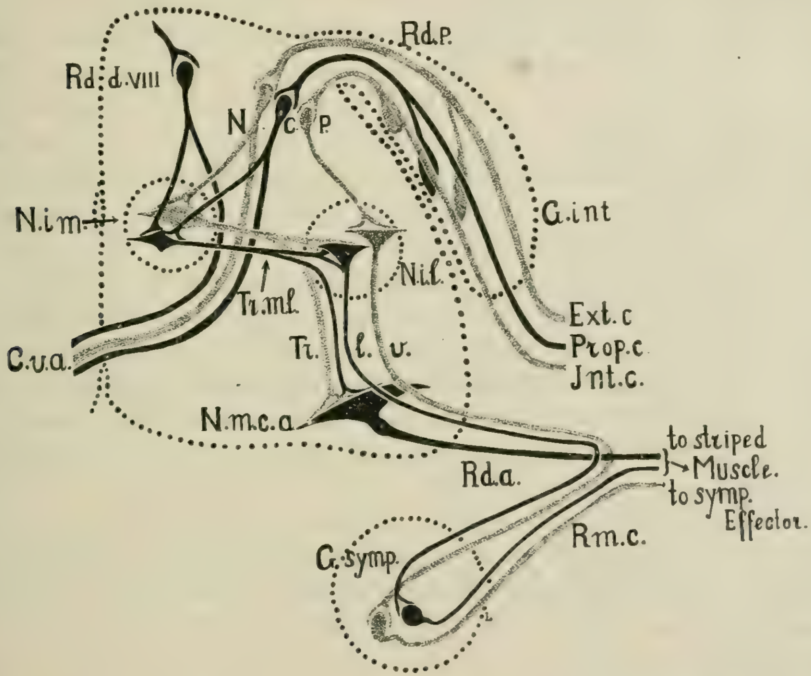

FIG. 6.—Scheme of the primary spinal reflex arcs. C.v.a., commissura ventralis alba. Ext.c., exteroceptor. G.int., ganglion intervertebrale. G.symp., ganglion sympathicum. Int.c., interoceptor. N.i.l., nucleus intermedio-lateralis. N.i.m., nucleus intermedio-medialis. N.m.c.a., nucleus motorius cornu anterioris. N.c.p., nucleus proprius cornu posterioris. Prop.c., proprioceptor. Rd.d.VIII, radix descendens nervi vestibularis. Rd.a., radix anterior. Rd.p., radix posterior. Rm.c., ramus communicans. Tr.l.v., tractus latero-ventralis. Tr.m.l., tractus medio-lateralis.

reflexes. The primitive exteroceptive reflexes elicited from the skin are, in our opinion, the nociceptive withdrawal reflexes, of which the simple flexion reflex is the most common type. The primitive proprioceptive reflex initiated in the motor apparatus itself is tonus. The labyrinth, in as far as its impulses help to maintain tonus, we associate for well-known reasons with the proprioceptive system. The primary spinal reflex arcs are, we believe, homosegmental, at least in those cases in which the primitive segmental character of the sympathetic system is still preserved. When, however, the outflow of the sympathetic fibres from the central nervous system contracts and becomes confined to the thoraco-lumbal part of the cord, this primitive character of the primary reflex arc is of course modified. Assuming that the primary reflex arc in the lumbal region of the frog's spinal cord is still homosegmental, we reproduce in our scheme only those elements which appear in a sequence of cross-sections of a single spinal segment. The new fact incorporated in this scheme is represented by the nucleus intermedio-medialis. (Cajal [5], Bok [3].) By the intermediation of the cells of this nucleus the stimuli reaching the cord by way of the posterior roots are distributed over the efferent sympathetic cells of the nucleus intermedio-lateralis and to the motor cells of the anterior horn, reaching first the efferent sympathetic cells and then the motor cells of the anterior horn. The nucleus intermedio-medialis is, therefore, the final common centre of the primary spinal reflex arcs.

In order that this scheme may not be misunderstood we call attention to the fact that the more complicated combinations of movements, especially progression and active attitude, are initiated by stimuli emanating from centres lying above the medulla oblongata. The fibres connecting these centres with the spinal motor centres enter the antero-lateral tract above the level of the primary motor centres where they terminate. These fibres are present in large numbers, but have been omitted in the scheme as not pertaining to the primary spinal mechanism. For the same reason there have been omitted the labyrinthine fibres that enter the antero-lateral tract above the level of the second spinal nerve, as well as all intersegmental associative fibres.

On the basis of this scheme we may now say more precisely what is meant by the word "local" in the term "local shock." On dividing the rami communicantes it is clear that shock affects, in the first place, the sympathetic efferent section of the primary spinal reflex arc, i.e., the nucleus intermedio-lateralis, and that when it spreads it reaches the nucleus intermedio-medialis. Similarily division of the posterior roots causes, in the first place, shock in the afferent section of the primary spinal reflex arc, i.e., in the nucleus proprius cornu posterioris ; then the shock extends to the nucleus intermedio-medialis. The fact that shock affects the nucleus intermedio-medialis after section of the rami communicantes, as well as on section of the posterior roots, is the reason of the close correspondence in the state of the animal immediately after those two operations.

In conclusion, I have to thank my colleague, Professor Zwaardemaker, who in the most courteous manner placed his laboratory at my disposal.

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THE CENTRAL CONNECTIONS OF THE VESTIBULAR NUCLEI WITH THE CORPUS STRIATUM, AND THEIR SIGNIFICANCE FOR OCULAR MOVEMENTS AND FOR LOCOMOTION.

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THE main facts about the cerebrofugal tracts have been known for some considerable time, but it is only of late that even a preliminary knowledge of the central ascending connections of the cerebral sensory nerves have been attained.

Monakow, Cajal, van Gehuchten, Probst, Horsley, O. and C. Vogt, and Sachs have pointed out the great importance of the thalamic nuclei as central stations for all corticopetal connections.

Wallenberg, Spitzer, van Gehuchten, and Hoesel were among the first to investigate the central connections of the more important sensory nerves—the N. trigeminus and N. vestibularis. As a result of these investigations a certain amount of light was thrown on the cerebropetal tracts of the N. trigeminus, but very little was learned about the central connections of the N. vestibularis. It is a curious fact that although physiological and anatomical data indicate the importance of these central connections, practically nothing was for long known about them. This is evident in Horsley's Boyle lecture of 1905, since in this lecture support is given to Mill's supposition that vestibular ascending connections arrive in the temporal convolutions. This view is, however, not accepted by Winkler, Kappers and Brouwer, who regard the lateral fillet as the pathway, or one of the pathways, for ascending vestibular stimuli to the higher cerebral centres. In 1914 [9] proof was forthcoming that the vestibular central connections pass upwards almost entirely in the posterior longitudinal bundle. A few pass from the nuclei tecti, where the cerebellar root of the vestibular nerve terminates, through the anterior cerebellar peduncle. Another tract may pass upwards from the nucleus ventralis raphé, but this is doubtful.

These few facts represented the sum of our knowledge of the central connections of the vestibular nuclei, and yet these connections are of the first importance for ocular movements, for equilibrium and for locomotion. Free locomotion and ocular movements in more than one plane are first seen in the lower vertebrates coincidently with the appearance of a vestibular organ, or some comparable apparatus, and with the development of a primitive corpus striatum.

From the clinical aspect, the regular appearance of typical disturbances of equilibrium of the cerebellar type in cases of tumour of the brain, and the presence of nystagmus and conjugate deviation of the eyeballs in variously localized lesions of the cerebral axis, indicate unmistakably the existence of ascending tracts from the vestibular nuclei.

The extraordinary importance of the subject and our very meagre information seemed to me sufficient excuse for this paper describing my work on the central connections of the vestibular nuclei, even if it be as yet incomplete.

Before passing to a description of my work and its results I would point out that the anatomical-physiological methods adopted by me in this and in earlier work [9] are not yet recognized by other workers.

Observations were first made by a series of lesions in the brain-stem of the cat. It was found that only lesions of the posterior longitudinal bundle resulted in forced movements in the horizontal plane (circus movement and conjugate deviation of head and eyes) and in the frontal plane (rolling movements and squint deviation of the eyes). Lesions elsewhere in the brain-stem were never followed by these types of deviation or movement.

Further, it was found that the direction of those forced movements was reversed when the lesion (hemisection) reached the region of the posterior commissure, and the nucleus commissuræ posterioris and nucleus interstitialis. From my observations these nuclei form the termini for the ascending fibres of the posterior longitudinal bundle after they have crossed in the posterior commissure. From these nuclei also originate the two descending tracts in the posterior longitudinal bundle (tr. commissuro-medullaris and tr. interstitio-spinalis or Boyce's tract).

It was also observed that a unilateral lesion of structures oral to these nuclei, involving the strands of fibres between them and the globus pallidus, was also followed by forced movements in the reversed direction. This phenomenon seems to be best interpreted by the assumption that nervous continuity exists between the two commissural nuclei and the globus pallidus.

In connection with this last observation, it is interesting to note that C. and O. Vogt [21], whose work is on purely anatomical lines, have also come to this conclusion, that a direct nervous connection exists between the commissural nuclei of the one side and the globus pallidus of the other. This partial anatomical confirmation of facts obtained by me with the anatomo-physiological method seems to be a valuable argument in its favour, and goes far to justify its adoption in attempting to trace the ascending vestibular tracts.

In an earlier paper [9] I pointed out that within the nuclear complex of the N. vestibularis in quadrupeds a very high degree of differentiation of function is attained. On each side of the median line are two nuclei, lesions of which cause circus movements but in different directions. Lesion of one of the nuclei produces circus movements to the same side, while lesion of the other is followed by circus movements to the other side. Injury of the tracts ascending from these nuclei to join the mesial part of the posterior longitudinal bundle also results in similar forced movements. Further, on each side of the median line lie two nuclei, injury of which causes rolling movements. These nuclei show the same differentiation as those associated with the circus movements, since a lesion of one results in the rolling movements being directed towards the affected side, while injury on the other is associated with rolling movements directed towards the opposite side. The ascending fibres from these two nuclei are localized in the lateral wing of the posterior longitudinal bundle.

It is important to note that in a cross section involving the whole of one longitudinal bundle, including as it does the fibres concerned with circus movements to both sides, the result is circus movement to the intact side, rolling movement to the affected side. If, however, the lesion is situated oral to the posterior commissure the circus movements and rolling movements are conversely directed towards the affected and the intact sides.

It is found in monkeys, cats and birds, that a lesion involving the nuclei tecti and their ascending fibres in the superior cerebellar peduncle is followed by the falling backward of the animal, or at least a conjugate deviation of the eyeballs upward. On the other hand if the lesion involves the grey matter near the raphé of the medulla (nuclei of the raphé) and the medial nuclei of the pons the result is a distinct tendency to fall forwards. Further, a lesion in this region of the human brain appears to be associated equally with nystagmus and a forced position of the eyeballs in the vertical plane.

Before passing to the main subject matter of this paper I would recall my earlier work of 1907 [8] where I demonstrated that the nucleus tecti receives direct as well as indirect fibres from the vestibular nerve. This was subsequently confirmed by de Villaverde [20]. These data on the anatomical, physiological relations of the vestibular nerve may form a basis for further investigation, for there is, as far as the Marchis-stain goes, evidence that no other ascending vestibular pathways exist. Careful workers consider the lateral fillet as a possible pathway for secondary vestibular tracts. This view they regard as being phylogenetically sound.

In the evidence which I offer for the solution of the problem I shall confine myself to one case in which the experiment may be regarded as crucial.

The experiment, which was performed on a cat, was carried out as follows: A protected needle, as devised by Probst, was used to pierce the medulla. This was introduced from behind on the right side and manipulated so that the vestibular region was completely destroyed (figs. 1 and 2). The needle pierced the lateral fillet at the level of the mesencephalon. On examination it was found that all the tracts described by me as secondary vestibular tracts were degenerated (fig. 3). The lateral fillet was quite free from any degenerative change up to the point where the needle pierced it (fig. 4). From this point marked degeneration extended right up to the end station in the thalamus (fig. 5). I repeated this experiment several times with the same result, viz., no degenerative changes occur in the lateral fillet from injury of the vestibular nuclei.

The result of these experiments is, in my opinion, sufficient to justify the conclusion that the fillét contains neither primary nor secondary vestibular fibres.

The next point for investigation is whether the physiological method used in the anatomical analysis of the primary and secondary vestibular connections will serve equally well for the elucidation of the tertiary vestibular connections. By tertiary vestibular connections are meant those tracts which connect the supra-nuclear centres (i.e., the nucleus commissuræ posterioris and the nucleus interstitialis) near the posterior commissure with the prosencephalon.

Theoretically no objection can be raised to the method, but the fact must be remembered that the physiological effect of a lesion of the ascending vestibular connections diminishes markedly the farther it lies from the entrance of the vestibular nerve. A second point is that the resulting forced movements vary in degree in different animals. Thus in rabbits they are very vigorous, but are much less when the same experiment is performed on animals higher in the scale. Thus in man a lesion of the ascending tracts causes only a forced position of the eyes, or a still less impressive phenomenon, a tendency to conjugate deviation ("Blickparese" of the Germans), or a tendency to fall or walk to one side when the eyes are closed.

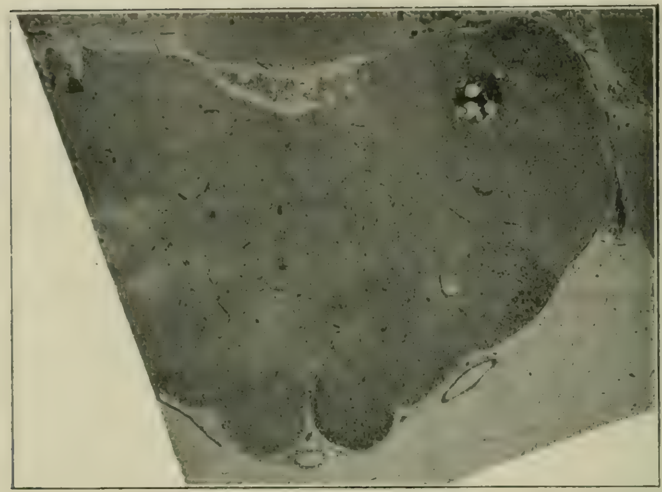
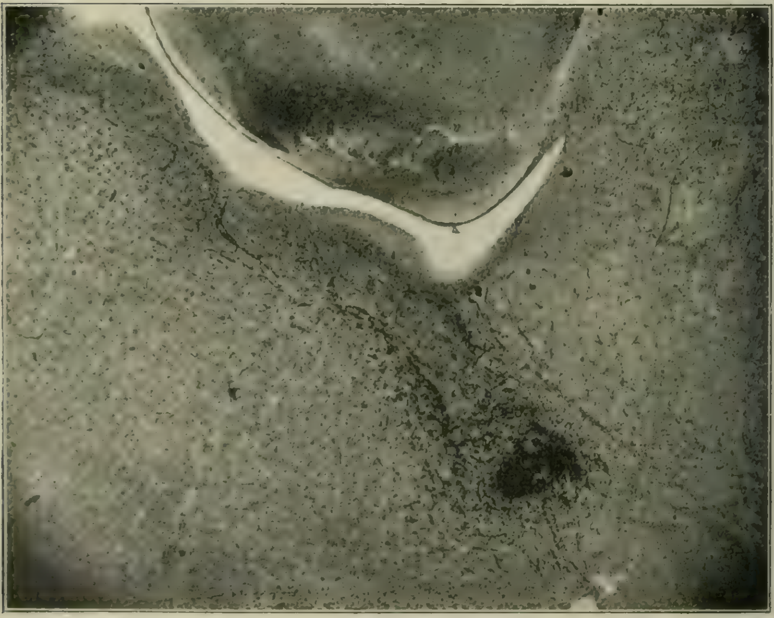


Fig. 1.



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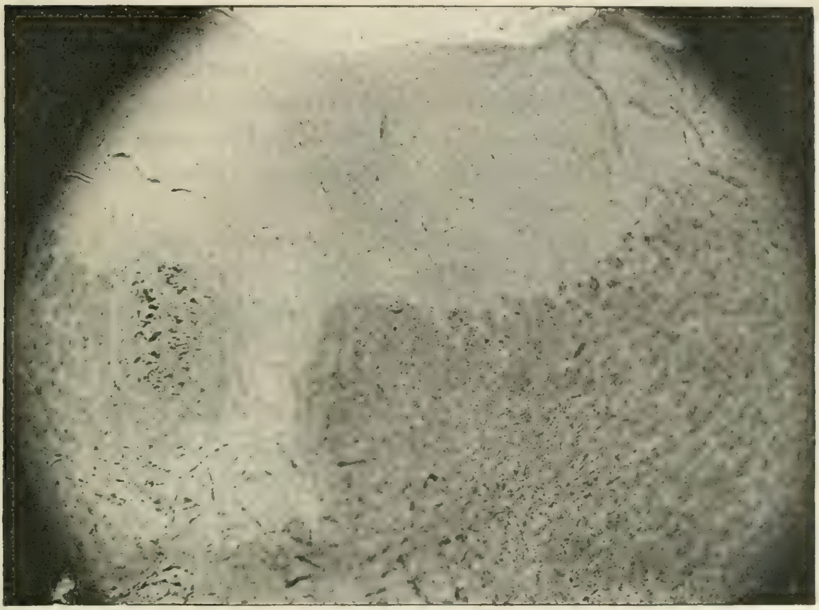

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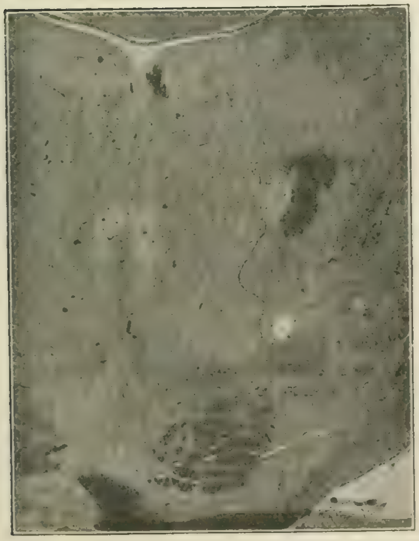

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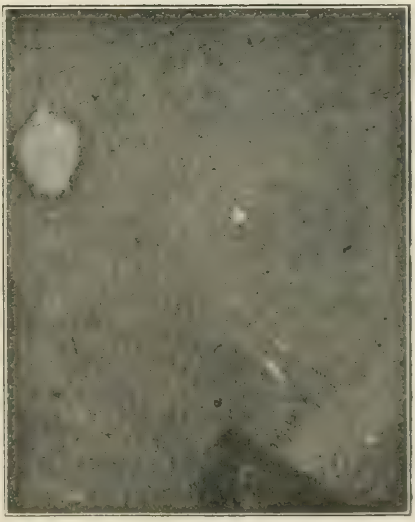


Fig. 5.

Figs. 1-5.—Cat. Lesion of the vestibular nuclei. Ascending degeneration in the posterior longitudinal bundle only. Note absence of degeneration in the lateral fillet.

Again, in quadrupeds section of the vestibular nerve causes, as a rule, violent rolling movements to the side of the lesion, whereas a lesion of the ascending connections of the vestibular nuclei in the midbrain (posterior longitudinal bundles) is followed merely by a tendency to fall towards the affected side. In the human subject even this may not occur, but there is a tendency to lie in bed on the affected side, or to lean over to that side when sitting up.

It is, therefore, not remarkable that the result of severance of the tracts connecting the supranuclear centre (nucleus interstitialis) with the prosencephalon should be only a slight tendency to fall towards the normal side. It must be remembered, however, that this symptom although slight is very constant. Further, after a lesion in the prosencephalon in quadrupeds, the circus movements which result are neither so marked nor so persistent as those seen after section of the mesial portion of the posterior longitudinal bundle. Sometimes this circus movement to the side of the lesion may last a few days only, especially if the lesion be slight, but there may be a tendency for some time for deviation of the head and eyes towards the lesion. In monkeys and in man regular circus movements never result, but there is a distinct tendency to look towards the lesion. If the subject be blindfolded and told to march there will be seen a clear tendency to deviate from the straight line.

Regarding forced movements in the frontal plane, after prosencephalic lesions in quadrupeds there is a tendency to fall towards the normal side, accompanied by a deviation of the eyeballs known as the "Magendie-Hertwig squint." In man both these symptoms must be looked for very carefully, or they are completely missed. Careful observation is necessary to detect forced movements in the sagittal plane (forwards and backwards) in quadrupeds, while in man their observation requires special attention. Consequently the physiological-anatomical analysis of the tertiary vestibular connections has to be carried out with the utmost circumspection and critical care.

When we take into consideration how little is known of the physiology of the corpus striatum it is not surprising that its significance as a vestibular end-station has only recently been recognized. Remarks in the literature indicate that attention has been attracted to the corpus striatum in cases of conjugate deviation and forced movements. Prevost [12] calls attention to the fact that when in apoplexy the apoplectic area involves the corpus striatum, conjugate deviation of the head and eyes towards the side of the lesion results. Prus [14] notes that when certain parts of the corpus striatum are stimulated electrically either pleurothotonus or elevation of the head results. Sachs [17] also records stimulation experiments of the same nature. Bechterew [1], who must be regarded as a pioneer in this work, records observations made by him of forced movements in dogs after lesions involving the base of the forebrain, and postulates the presence of vestibular centres in this region, although he does not mention the corpus striatum.

In experiments carried out by me on cats I found that lesions involving the region of the hypothalamus, the lamina medullaris ventralis and the globus pallidus were followed by circus movements to the side of the lesion and rolling movements to the normal side. Lesions involving other parts, as the anterior and median thalamic nuclei, or the anterior corpora quadrigemina, corpus geniculatum and corpus callosum, never gave rise to forced movements of any description.

The difficulties attending anatomical investigation of this region are very great. Dejerine and Horsley with their co-workers rendered valuable assistance to the investigation of nerve tracts by their application of the Marchi method. At the same time when an effort is made to extend the older physiological work of Majendie, Schiff, Probst and others, the difficulties, which of necessity beset so delicate an investigation, at once become apparent. The physiology of such regions as the red nucleus, the posterior commissure, the hypothalamus, the palæostriatum (globus pallidus, nucleus accumbens, area parolfactoria) and the neo-striatum (putamen and nucleus caudatus), is still a matter of conjecture. It can readily be understood how extremely difficult it is to produce sharply localized lesions in these regions. The formation of a thrombus may throw out of action a much larger area than is desired, and the direction or shape of the thrombus plays an important part. At the present time one cannot eliminate the element of chance from such experiments, but out of a series a few useful results may be obtained.

I now propose to discuss a series of sections prepared from the brains of a rabbit and a cat. The sections from the rabbit were prepared in the Central Brain Institute and were stained by the Weigert-Pal and van Gieson methods. The sections from the cat were stained by the Marchi method.

In both cases the posterior commissure was pierced by a needle (rabbit, fig. 9; cat, figs. 15 and 16) and the grey matter in front and on the mesial side of the red nucleus (region of the nucleus interstitialis) was divided. In the cat the central grey matter of the aqueduct and the nuclei of the posterior commissure (Darkschewitchi) were also injured. The rolling movements which resulted in both cases appeared immediately after the operation, diminished after a few days, finally showing themselves only in a persistent tendency to fall towards and to lie on the normal side. Circus movements to the side of the lesion resulted only in the case of the cat and persisted for a few days only.

In the case of the rabbit, which survived for six months after operation, careful observation failed to discover any tendency to turn to one side more than another; it was highly probable, therefore, that Darkschewitchi's nucleus, which is associated with circus movements, escaped injury. Forced movements in the antero-posterior plane were seen in the cat only, and appeared as stepping and staggering movements. They were only present for the first few days after operation, and were probably due to lesion of the nuclei near the middle line.

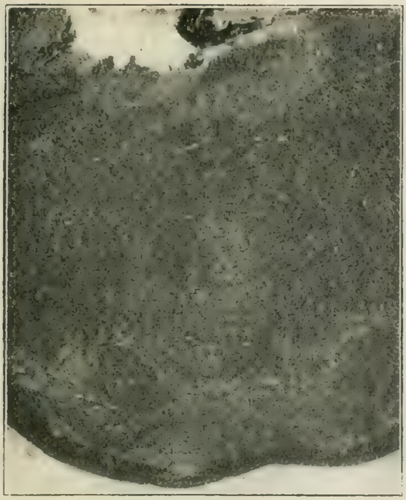
The forced position of the eyes in both animals was that which usually accompanies the phenomenon of rolling movements to the right [5]. Both eyeballs were rotated round the visual axis towards the right side, the right eye being directed downwards, the left upwards.

It is interesting to note that both animals appeared to be blind immediately after operation, probably owing to the cross-section through the dorsal division of the posterior commissure. Later this passed off but hemianopsia towards the right persisted in both.

Microscopical examination of the brain and spinal cord of the cat showed the extent of the injury to be as follows.

The lesion in the middle line extended so far back that both bundles of Monakow were severed at their crossing, and they were consequently degenerated down to the lower segments of the cord. Both pyramidal tracts showed degeneration; the left was injured in the motor cortex as a result of the primary lesion, and also where the needle after piercing the midbrain reached the pes pedunculi.

The primary and secondary degenerations found in the posterior longitudinal bundles and the posterior commissure, with its nuclei and their connections, are particularly important. As these degenerations are for the most part identical in the rabbit and the cat, the fact that the Weigert-Pal and van Gieson methods were used in the one case and the Marchi method in the other makes the physiological and anatomical comparison of the two series more interesting.



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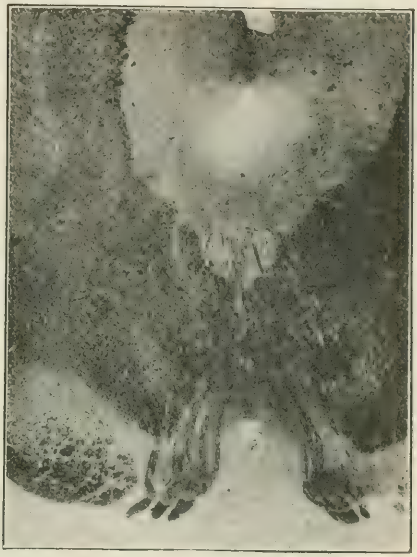

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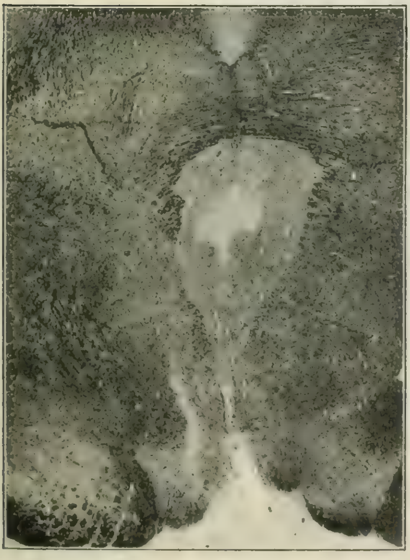

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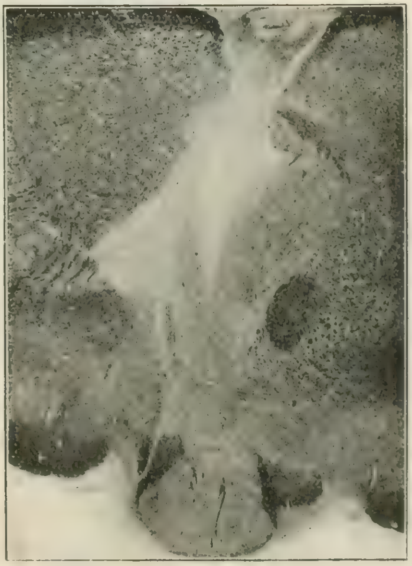
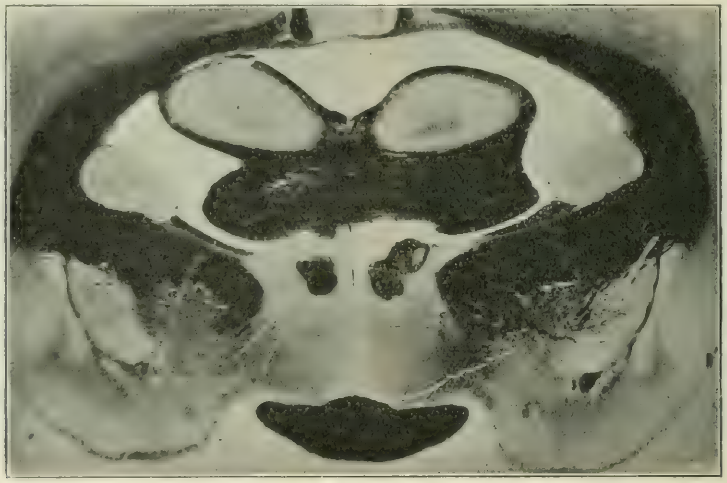


Fig. 9.

Examination showed complete division of the posterior commissure. This is a lesion rarely described in literature, but was noted by Probst [13], Buzzard and Collier [2]. In the rabbit the secondary ascending vestibular tracts in the posterior longitudinal bundles were divided. In the cat the lesion was more limited to the middle line. It was found that on the left side (the side of the lesion) both the commissuro-medullaris and the interstitio-spinalis (Boyce's tract) tracts were degenerated



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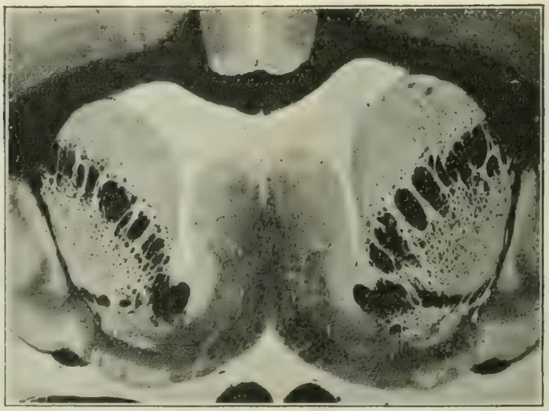
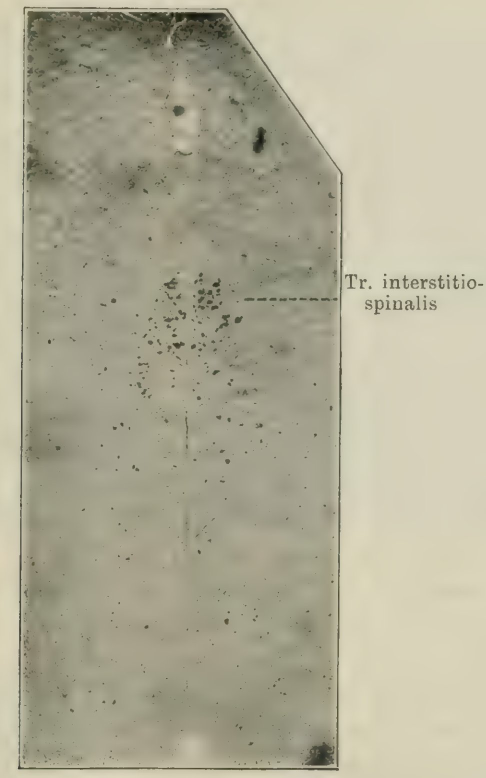


Fig. 11.

Figs. 6-11.—Rabbit. Lesion of the commissural nuclei on the left side. Descending degeneration of the mesial part of the left posterior longitudinal bundle, and of the lateral horn of the right posterior longitudinal bundle. The left globus pallidus is diminished in size.



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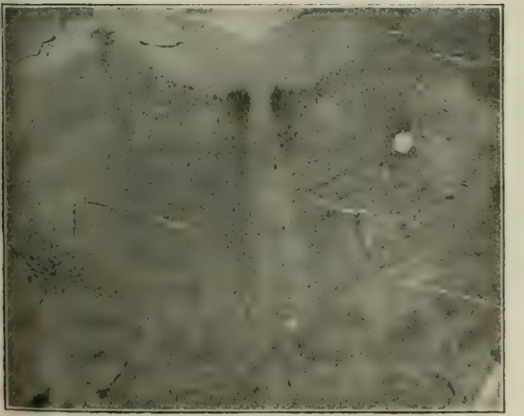

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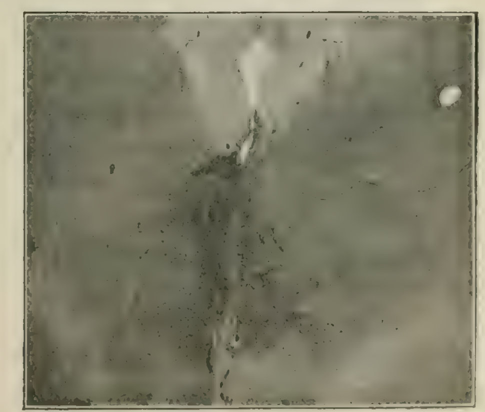

Fig. 14.

(figs. 12, 13). The lesion crossed the middle line, injuring the right posterior longitudinal bundle, and the interstitio-spinalis tract of this side also showed degeneration (fig. 14).

In the rabbit the left posterior longitudinal bundle in the medulla oblongata, particularly in its median portion, was less prominent than on the right side (fig. 6). In the pontine region this difference was less noticeable. It appears probable, therefore, that in this case the nucleus commissuræ posterioris suffered less injury, and as a result the commissuro-medullaris tract.

The most important point in these two experiments is that they afford an opportunity for seeing the orally situated structures with which the mesencephalic nuclei are connected.

In the rabbit, where rolling movements alone were seen, the lesion of the commissural structures was more limited. With the Weigert-Pal stain the corpus striatum presents the same picture as that described by Monakow in a rabbit [7]. These histological changes are as follows: The entire left globus pallidus, less so the putamen, but not the nucleus caudatus, show a decidedly atrophic appearance, compared with the normal side. Forel's field on the affected side is also rather thin, while the lamina medullaris externa thalami is not at all prominent (figs. 9, 10).

In the cat (241) the Marchi stain demonstrates the course of the striopetal fibres from the commissural nuclei. In following the fibres from the commissural region it is seen that the crus cerebelli ad thalamum of the left (side of lesion) is the more prominent; the majority of its fibres disappear orally in the neighbourhood of the lamina dorsalis thalami (fig. 16). From the capsule of the red nucleus a number of degenerated fibres pass at first ventrally, then laterally, in the direction of Forel's field. The lamina medullaris externa is thickly dotted with fine black spots (fig. 17). It is certain that a number of degenerated fibres are lost in the body of Luys's nucleus, in Forel's field, and probably also in the middle and anterior thalamic nuclei. The majority, however, of these ascending fibres, which are in all probability mostly vestibular, disappear in the direction of the globus pallidus (fig. 18). The external capsule of the putamen, especially in its anterior part, is markedly degenerated. In the putamen proper there is very little evidence of degenerated fibres. Fig. 18 shows the capsule on the right side, where, however, the degeneration is not nearly so great as on the left side, where the commissural nuclei are completely destroyed. It was impossible to obtain a satisfactory photograph of the left side.

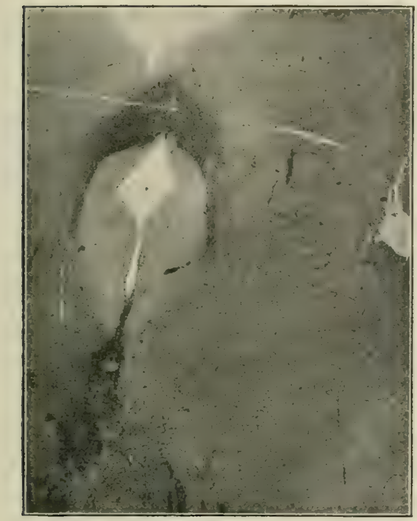

Fig. 15.

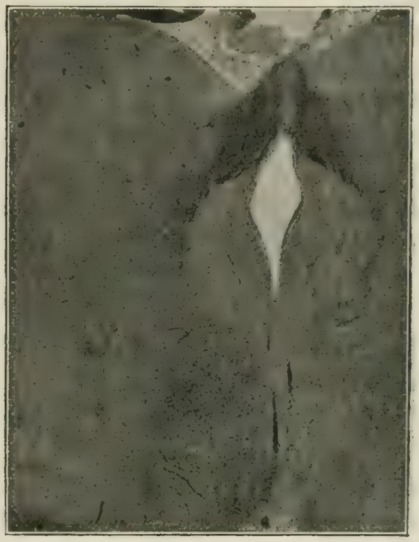

Fig. 16.

Fig. 17.

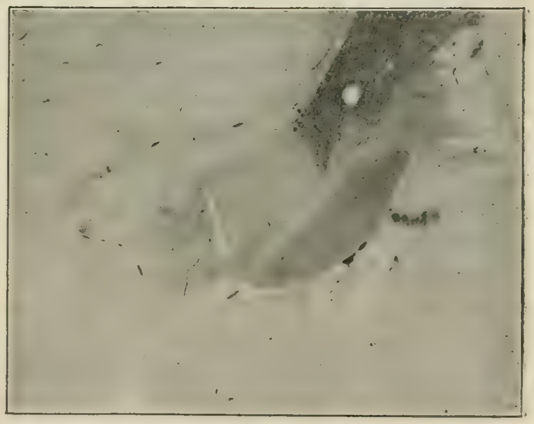

Fig. 18.

FIGS. 12-18. — Cat. Lesions of the commissural nuclei, mainly of the left side. Descending degeneration of the interstitio-spinal tracts, and less so of the commissuro spinal tracts. Ascending degeneration towards the globi pallidi, mainly on the left side.

These facts confirm results obtained by me in experimental work on cats. In some of these animals the globus pallidus itself was injured, or the lamina medullaris externa was severed. In such cases histological examination shows degeneration of fibres to the commissural nuclei and red nucleus on the one side, and to the globus pallidus on the other. Further, they agree with the anatomical observations of Wilson [23], who with the use of Clarke's apparatus demonstrated the existence of fibres passing from the putamen to the region of the globus pallidus and thence towards the capsule of the red nucleus.

I therefore conclude from this evidence that the commissural nuclei are in neuronal continuity with the globus pallidus of the same side. This connection consists of at least two neurons between the globus pallidus and the commissural nuclei, whereas in the reverse direction but one neuron exists.

These results may appear unexpected to the physiologist and the clinician, but if the work of Bechterew, Probst and Dejerine [3] is carefully considered, it is evident that considerable support for the results is forthcoming.

In the last section I called attention to the agreement in many points between my work and that of Wilson. In certain particulars, however, we differ. Wilson speaks of connections from the region of the globus pallidus passing to the region of the red nucleus. In all my experiments the red nuclei were intact, and it is extremely probable that the bulk of the globus pallidus connections do not reach the red nucleus at all, but pass to the two nuclei situated anteriorly and medially to it. It is probable that this investigator did not realize the existence of the nuclei commissuræ posterioris and interstitialis and their descending tracts in the posterior longitudinal bundle.

It is important when considering results obtained by other workers to remember that the application of the nomenclature differs somewhat in different countries. The English workers apply the term "ansa lenticularis" to the whole of the mass of fibres lying between the commissural nuclei, the red nuclei and corpus striatum, and more particularly to those fibres which penetrate the internal capsule to join the globus pallidus. Monakow, Winkler, Potter, Dejerine and his school apply the name only to the fibres lying between the mesencephalic nuclei and the more anteriorly situated parts of the corpus striatum.

It is not my intention to discuss afresh in detail the physiological points as applied to the human subject raised in this and in my earlier paper [9] in which an anatomical-physiological investigation of the posterior longitudinal bundle revealed only two descending tracts in its median part. One passes down from the nucleus commissuræ posterioris (tractus commissuro-medullaris) and is associated with circus movement and conjugate deviation of the eyes to the same side ; the second tract passes down from the nucleus interstitialis (tractus interstitio-spinalis, Boyce's tract) and is associated with rolling movement and the development of the Majendie-Hertwig squint. In this paper (p. 418) I concluded thus : "If this symptom (tendency to fall to the right) is present where the disease is localized cephalad to the posterior commissure, then from experimental findings the lesion is to be localized in the optic thalamus or striate body on the left side." When this was written I had already made use of the direction of these forced movements for purposes of localization in brain disease, particularly for diagnoses of frontal diseases.

It is interesting to find that in war literature is the first, and I think, decisive confirmation for this solution of the localization problem. Gerstmann [4], writing in 1916, published six cases of unilateral lesion of the frontal brain. In all the cases there was a disturbance of equilibrium demonstrated as a falling to the healthy side. The writer of the paper was evidently unaware of my paper (1914), and therefore could not appreciate the confirmation given to my suppositions. I therefore regard this falling to the healthy side as an important diagnostic sign in disease of the frontal lobe, or, to state it more exactly, of involvement of the globus pallidus or its connections with the commissural nuclei. Further experimental as well as clinical evidence seems to show that only in lesions of the globus pallidus do lasting circus movements and conjugate deviation of the eyes to the side of the lesion or a tendency to fall over to the healthy side result. From this one must admit continuity of anatomical connections from the vestibular region upward through the brain-stem to the globus pallidus. It must be remembered that a lesion of the putamen alone causes these disturbances for a short time only.

SECTION II.

Pathological lesions in man comparable to the above experimental lesions in cats and rabbits are rare.

In the Brain Institute in this city I found nothing to correspond with them. My attention, however, was drawn to a series of sections of the brain of a case of Meer en Berg, where a thrombotic process had caused atrophy of a great part of the left hemisphere.

The cortex of the entire frontal and parietal region was reduced to a thin lamella in which no traces of the convolutions could be detected. The corpus callosum was atrophied. The left lateral ventricle was enormously distended. Of the left corpus striatum the nucleus lentiformis was completely absent, and no part of the left putamen could be considered normal, and only a small number of cells were found in the globus pallidus. As this case has been discussed for other purposes and drawings of sections of it published [19], I shall limit myself to a statement of those details which are of importance for the present research.

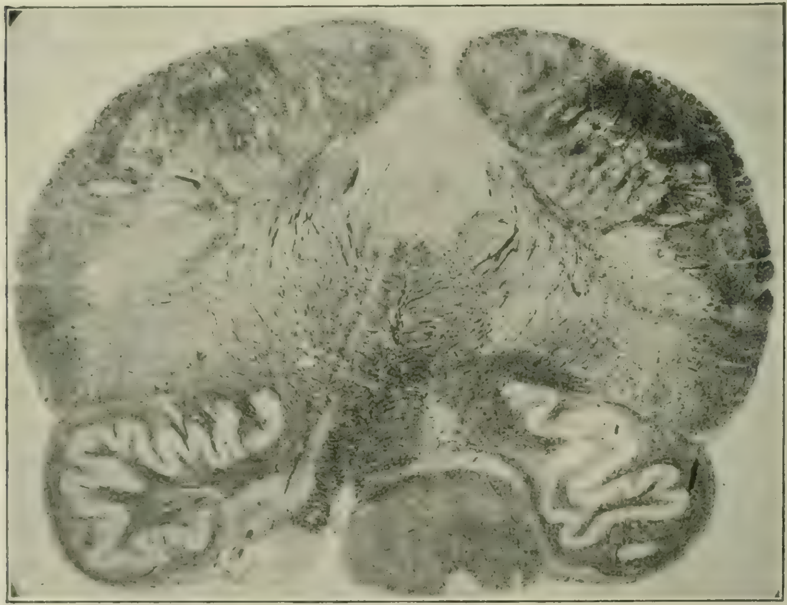

Fig. 19.

In the first place I would direct attention to the difference in size of the posterior longitudinal bundles, that on the side of the lesion being diminished (figs. 19, 20, 21, 22, 23). This difference in size must be explained by the interdependence of the globus pallidus and the homolateral nuclei (nucleus interstitialis and nucleus commissuræ posterioris), as has been shown experimentally in the rabbit. This being so, partial destruction of the globus pallidus is inevitably associated with atrophy of these nuclei and insufficient development of the homolateral fibres descending in the posterior longitudinal bundle [9].

The work of Edinger, Ramon y Cajal and my own unpublished observations on the constitution of the ventral part of the posterior commissure, would show that those nuclei receive afferent impulses from the heterolateral branch of the commissure, this being the continuation of the lateral horn of the posterior longitudinal bundle. It is therefore not surprising to find in this case that the right arm of the commissure contained fewer fibres than the left (fig. 22).

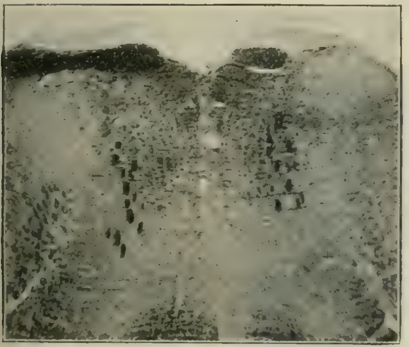
Fig. 20.

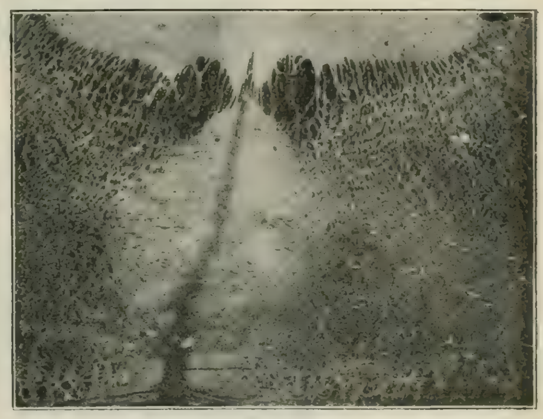
Fig. 21.

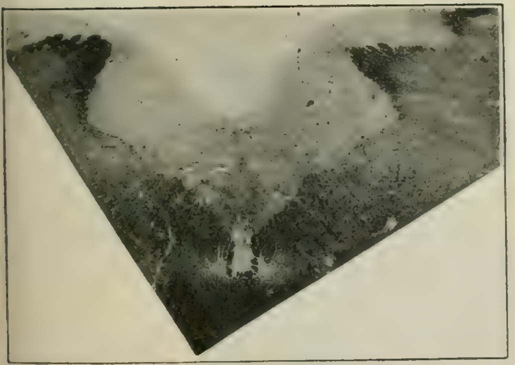
Fig. 22.
Note the fewer fibres in the mesial part of the left posterior longitudinal bundle.

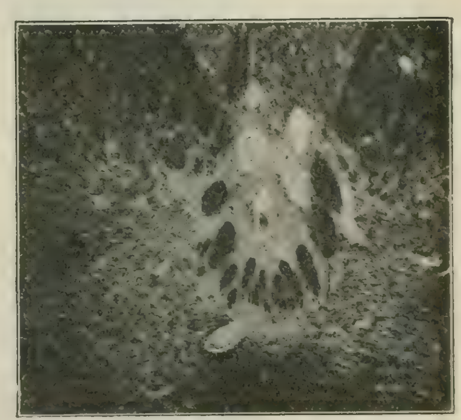
Fig. 23.
A portion of fig. 22 photographed under a higher magnification.

This case is comparable with the experimental rabbit; in the rabbit

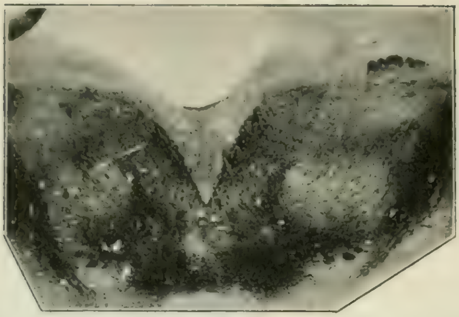

Fig. 24.

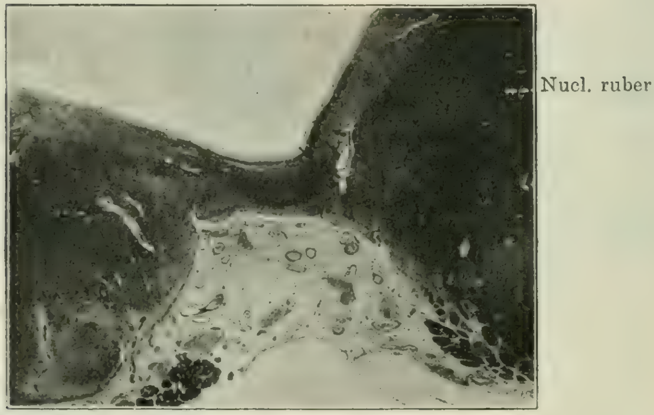

Fig. 25.

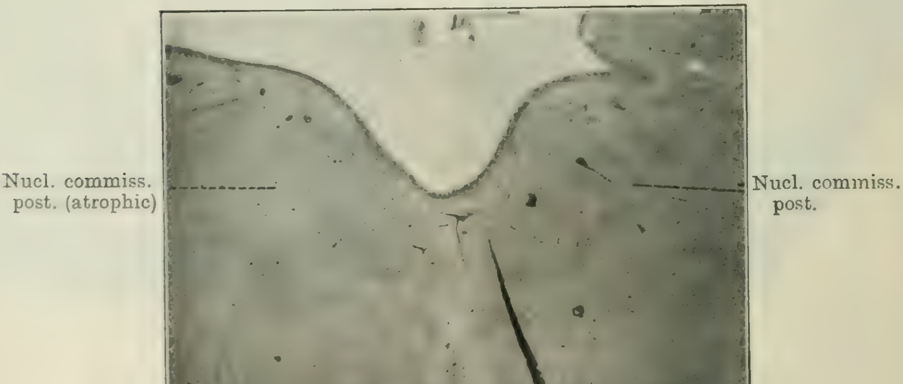

Fig. 26.

Figs. 19-26.—Section of a human brain in which a destructive lesion of the left corpus striatum had occurred several years before death. The left nucleus commissuræ posterioris and nucleus interstitialis are atrophic. Poverty of fibres in the lateral horn of the right posterior longitudinal bundle, and in the corresponding part of the posterior commissure. In fig. 19 note the smallness of the left posterior longitudinal bundle owing to absence of the tr. interstitio-spinalis.

the lateral wing of the posterior longitudinal bundle on the side of the lesion involving the commissural nuclei was more voluminous than on the other side (fig. 6). In the human brain destruction of the left globus pallidus is also associated with a greater development of the lateral wing of the left posterior longitudinal bundle (fig. 21).

From these facts we must recognize a cerebropetal structural and functional continuity between the left corpus striatum, the right arm of the posterior commissure and the lateral wing of the right posterior longitudinal bundle. Further, it is also found that the left corpus striatum is cerebrofugally connected with the commissural nuclei, and by means of these with the descending fibres in the innermost part of the mesial segment of the left posterior longitudinal bundle.

Finally I would direct attention to the red nucleus.

When the series of sections are examined from below upwards it is found that these nuclei first appear in the same cross-section (fig. 24). It is probable, therefore, that the caudal parts at least of these nuclei are not dependent on the corpus striatum of the same or the other side.

In fig. 25 the frontal part of the right red nucleus is seen, but of the left there is no trace. It would, however, be premature to conclude that the frontal part of the red nucleus has a special relation to the homolateral corpus striatum, since the exact homology of those regions is unknown. The difference in the oral parts of the red nuclei might be due to the fact that in man the nucleus interstitialis is represented by the frontal part of the red nucleus.

From further experimental work I maintain the conclusions put forward in my former paper [9], that the nucleus commissuræ posterioris and the nucleus interstitialis represent superimposed vestibular nuclei. These nuclei receive their stimuli from the ascending elements of the crossed posterior longitudinal bundle via the posterior commissure. The descending fibres from them, the tractus commissuromedullaris and the tractus interstitio-spinalis, are situated in the mesial division of the posterior longitudinal bundle. The descending fibres or tracts are concerned with locomotion in two planes (circus movement with conjugate deviation of head and eyes, and rolling movement with Hertwig-Majendie squint).

It must be admitted that for some reason a lesion of the ascending elements of this vestibulo-motor nerve chain prevails in its effects over lesions of the descending elements. This is shown by the fact that in a series of hemisections from the pons upwards the direction of the forced movements changes as soon as the posterior commissure is reached. Further, the supra-nuclear centres are connected with the corpus striatum, or at least with the oral part of the globus pallidus. The direction of the forced movement does not change wherever the supra-nuclear section is made. If an animal with a lesion in this part survives sufficiently long some loss of fibres may be found in the mesial part of the posterior longitudinal bundle, and also in the wing of the posterior longitudinal bundle of the crossed side. This descending degeneration has been observed in the case of a patient of my own with recent destruction of the globus pallidus, and also in similar cases recorded by Dejerine and Roussy [16].

SECTION III.

My earlier work on this subject [9] indicated that the commissural nuclei (N. commissuræ posterioris and N. interstitialis) as well as the secondary, and perhaps tertiary, vestibular tracts which compose their afferent systems, are concerned exclusively with locomotion and conjugate deviation of the head and eyes in the horizontal and frontal planes. It is proposed to give here a short note on the fibres and nuclei which subserve forced movements in the sagittal plane, that is locomotion and conjugate deviation of the head and eyes upwards and downwards.

The nuclei and fibres which determine forced movements in the horizontal (circus movements) and frontal (rotation round the body axis) planes are situated symmetrically on either side of the middle line, one system co-ordinating the deviation or rotation to the right, the other to the left. Physiological and clinical data tend to show that entirely different nuclei and tracts determine vertical deviations. This is not surprising since the one set of movements—standing up, looking upwards, falling backwards, going backwards—is not the reflected image of the other set—stooping down, looking down, falling forward, going forward.

The upward and downward forced movements are never of the violent character seen in rabbits when the vestibular nerve has been injured. Further, they seem very easily compensated. During the first few days after operation on the cat (241) there was a tendency to recoil, to fall backward and to go backward, and a very slight pressure under the chin caused the animal to sit up. This form of forced movement in the sagittal plane invariably follows a lesion of the nucleus tecti cerebelli in the cat and the pigeon. It is interesting to find that there is some clinical evidence on this point, similar forced movements occurring in cases of tumour of the cerebellum involving the nuclei tecti.

Wallenberg [22] working with pigeons found that after lesions of the superior cerebellar peduncle there was a tendency to retrogression, and thought that injury to some nucleus in this region was associated with the development of these movements. Marburg, Bing, and Ingvar also found that lesions of the spino-cerebellar tracts in animals were associated with disturbances of locomotion in the antero-posterior direction.

In 1907 I described the terminations of fibres of the vestibular nerve in the nucleus tecti. It seems highly probable that the nucleus tecti plays the same part in forced movement in the antero-posterior direction as Deiters' nucleus and the descending vestibular nucleus do in circus and rolling movements. The fact that the ventral and dorsal spino-cerebellar tracts terminate in the nuclei tecti seems to corroborate this view [10].

In a series of sections through the brain of the cat (241), already referred to, a tract of degenerated fibres is seen on both sides of the section lying on the inner side of the anterior cerebellar peduncle (fig. 13). The position of this tract is almost identical with the hook-like structure found by Russell [16] in dogs after a median incision between the nuclei tecti. This structure was also described by Thomas [18]. The difference between my case and the cases of Russell and Thomas is that in their cases the degeneration was cerebello-fugal while in mine it is cerebello-petal. This in no way serves as an argument against my view but is rather evidence in favour of it, since from the time of Held [5], who first drew attention to the fact, it has been more and more appreciated how frequently the ascending and descending secondary and tertiary vestibular pathways lie in the same areas.

At present we can only surmise which supra-mesencephalic nucleus receives these fibres, but probably it is situated ventrally to the posterior longitudinal bundle in or near the raphé. This suggestion is made from a study of the rabbit already described where the structures of the median line were intact, and where no trace of forced movements in the vertical plane occurred.

Physiological and clinical observations therefore tend to show that a lesion near the median line in the thalamic region will cause staggering, and walking or falling backward, as do lesions of the prosencephalon if not situated too ventrally.

It seems justifiable to assume ascending connections similar to the tertiary striatal connections of the commissural nuclei, but passing to the palæostriatal nuclei septi.

Although experience has shown the utility of the physiological-anatomical method it must be understood that great care is necessary in its application. This is particularly so in attempting to demonstrate the tertiary vestibular connections where conclusions have to be drawn from transient and puzzling forced movements in the antero-posterior or sagittal plane. The forced movements in this plane are never violent even after lesions of the primary connections. It is also important to remember that the forced movements in the other planes (circus movement and rolling) decrease in strength the farther the lesion is from the primary vestibular fibres.

I may say in conclusion that I have carried out certain experiments and collected some clinical data on the position of the vestibular nuclei, the superimposed nuclei and their connections which may excite forced movements in the sagittal plane in the opposite direction to those already described, i.e., falling forward and locomotion forward. There is some evidence that the nucleus ventralis raphé is associated with this type of movement. In one experiment where the lesion involved the basal longitudinal bundle (Wallenberg) near its origin in the frontal brain the animal never sat up again in a natural manner, but held its head down. It may be surmised that the secondary tracts run up near the raphé and are situated somewhat ventrally. Further it seems probable that the tertiary ascending and descending fibres dealing therewith are to be found in the area of the basal longitudinal bundle of Wallenberg.

SUMMARY AND CONCLUSIONS.

(1) Persisting circus movements and lateral conjugate deviation of the head and eyes to the affected side, and a tendency to fall to the normal side after cerebral lesions, is due to injury of the oral part of the globus pallidus, or of its connections with the commissural nuclei (nucleus commissuræ posterioris and nucleus interstitialis). Hence the conclusion seems warranted that the tertiary vestibular tracts, lesions of which produce the same symptoms, terminate in this palæostriate centre.

The secondary vestibular tracts which ascend in the posterior longitudinal bundles cross the middle line by way of the posterior commissure before entering the nucleus commissuræ posterioris and nucleus interstitialis. In the diagram in my earlier paper [9] these ascending vestibular tracts were wrongly indicated as terminating in the commissural nuclei before crossing the middle line.

(2) It has not been possible to determine by the anatomical-physiological method the chains of neurons concerned in forced movements in the sagittal plane, i.e., recoil, retrogression, conjugate deviation of the head and eyes upwards; falling forwards and deviation of the eyes downwards. Experiments on cats, in which lesions of the nucleus tecti and of the superior cerebellar peduncle produce a tendency to recoil, recall the experiments on pigeons by Wallenberg, who assumed the existence of some such centre in or near to the superior cerebellar peduncle. Clinical and physiological observations lead us to suppose that structures exist in the mesencephalon, near the raphé and ventral to the posterior longitudinal bundle, lesions of which cause falling backwards and deviation of the eyes upwards. There is also experimental evidence that lesions of the palæo-striate nucleus septi (Kappers, de Vries) cause recoil and retrogression.

Near the middle line but more ventrally situated there are structures (? the basal longitudinal bundle of Bischoff and Edinger), lesions of which produce a tendency to fall forwards and deviation of the eyes downwards.

I have to acknowledge my indebtedness to Dr. Ariëns Kappers and Dr. Brouwer for their permission to make use of the material of the Central Brain Institute in Amsterdam, and to Mrs. Shaw Dunn for her kind help in correcting the English of this paper.

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Proceedings of the Section of Neurology of the Royal Society of Medicine.

CLINICAL MEETING, NOVEMBER 9, 1922.

Dr. WILFRED HARRIS, President, in the Chair.

(1) *A Case of Tremor of Rare Nature.*

By Dr. ANTHONY FEILING.

Gladys C., aged 10½, was brought to the hospital on account of involuntary movements of the left side of the body. She was a full-time child, a breech presentation and at birth had white asphyxia. Sat at 18 months, walked at 3 years. Has never had fits or other illnesses, except measles.

At the age of 9 months involuntary movements were noticed on the left side of the body, and weakness in holding up the head. During the last six months these movements have become worse and have extended to the other side of the body. At times her voice is very feeble. No history of any nervous disease in the family. The child is well grown and appears quite intelligent.

There is a slight weakness of the lower part of the right side of the face, while the tongue is deviated slightly to the left. The left arm is the seat of a rhythmical tremor, more marked in the proximal parts of the limb. The movements produce rotation of the arm at the shoulder, pronation and supination of the forearm, and flexion and extension of the fingers. The rate is about two to the second. Both arms are hypotonic.

Similar movements affect the trunk and the legs, though to a less extent. In the legs also the proximal muscles are involved to a greater extent than the distal. There is no actual paralysis, though the power of the left arm and leg is less than in the right limbs. The deep reflexes are present and the plantar responses are flexor.

(2) *Parkinsonian Syndrome associated with Right Hemiplegia, showing Peculiar Disturbances of Tone and Posture in the Limbs on the Hemiplegic Side.*

By Dr. DOUGLAS MCALPINE.

Patient, a female, aged 20, was quite well until April 18, 1919, when she developed a typical attack of encephalitis lethargica, complicated from the outset by a right hemiplegia. Her present condition developed gradually within a few months from onset.

The following is a brief summary of her present condition :—

Parkinsonian facies, smile and speech, with slight right hemiplegia and definite extensor response on right side; on left side doubtful extensor response. Power quite good all four limbs; no sensory disturbances.

At the proximal joints in all four limbs there is a slight resistance to both flexion and extension by passive movements, most marked in the lower limbs. If the fingers or wrist of the right hand be passively moved into any position, such position is maintained involuntarily. Right ankle when inverted or everted remains in that position; this is not seen however in dorsal or plantar flexion at proximal joints, nor in the limbs on the left side.

Voluntary movements.—Extension at elbow is possible only when fingers are extended: with the fingers flexed there is always accompanying pronation; extension of fingers is possible only when patient voluntarily abducts the arm, flexes the elbow, pronates the forearm and flexes wrist, or when she extends the hyperpronated elbow. The postures of hand and wrist on voluntary movement of the limb tend to take one of four patterns :—

(1) Flexion of fingers and wrist. (2) Extension of fingers and thumb, wrist being flexed or slightly extended. (3) Extension of wrist and first phalanges, with flexion at interphalangeal joint and apposition of thumb. (4) Same position of fingers as in (2), but with flexion of the wrist and pronation of the forearm. The position of the elbow is variable.

All voluntary movements of the hand are carried out slowly and with difficulty. The phenomenon of tonic innervation is well seen in the right hand and wrist. If patient when grasping the observer's hand is then told to relax her grip she is unable to do so for a period varying between fifteen seconds and two minutes; she has to manœuvre her arm into the position described as necessary when extending the hand. This condition is not seen at the proximal joints, but occurs to a slight extent at the right ankle. There are no athetotic movements, nor motor apraxia. A flexion and sometimes an extension reflex (as described by Riddoch and Buzzard) is obtainable in both upper limbs when a nocuous stimulus is applied to either extensor or flexor aspect of arm.

On assuming the upright posture the right arm at once becomes extended at elbow, hyperpronated, flexed at wrist and deviated to the ulnar side, with fingers flexed into palm. As soon as right foot touches the ground it becomes powerfully inverted, with plantar flexion of foot and toes, but the hallux is dorsiflexed so that the pad of the toes alone touches the ground; at the same time there is extension of the knee. After half a minute or so the tonic spasm of the foot gradually relaxes and the right foot assumes its correct posture on the ground. On attempting to walk the right leg is overflexed at the hip and the whole leg goes into extensor spasm again, the attitude of the leg at this stage resembling that depicted in the goose-step of the German soldier. Gradually the right leg is lowered and toes approach the ground; then, as spasm relaxes, the heel is gradually lowered until it touches the ground, the weight meanwhile being transferred to right leg. As the right leg is carried forward the right arm, maintaining the posture described above with palm turned outward, is powerfully retracted and abducted at shoulder, and as the patient transfers her weight on to the right leg the right arm comes forward again into line with the body.

Remarks.—In this case there is evidence of a moderately well developed condition of Parkinsonian rigidity associated with a slight right hemiplegia, and in all probability with some disturbance of the left pyramidal tract, as evidenced by the nature of this plantar response and the presence of a well-marked flexion reflex in the left upper limb; despite this bilateral pyramidal involvement there is an entire absence of pseudo-bulbar symptoms. There is no evidence that the phenomenon of tonic innervation depends on a lesion on a higher plane than the internal capsule, which however was the case in seven out of the nine cases collected by Wilson and Walshe. The condition seems to indicate lack of reciprocal inhibition of antagonists, so that one muscle group remains contracted despite volitional attempts to innervate the opposing group of muscles. In this case apparently the same phenomenon is present both on voluntary and on passive movement, and in the maintenance of a posture of right hand brought about by the observer; therefore no separation is possible between the phenomena occurring on voluntary and involuntary movement. It seems certain that in this case the condition of tonic innervation can be explained by a central lesion resulting in a disturbance of reflex tonus. The posture which develops in the limbs on the right side on standing or attempting to walk is clearly determined by the assumption of the upright position, and resembles closely the antigravity posture as described by Sherrington in the decerebrate animal.

I am indebted to Dr. Campbell Thomson for permission to show this case.

Dr. RIDDOCH, referring to the flexion reflexes of the upper limbs, said they were similar to those observed by Buzzard and himself in hemiplegia due to cerebral and spinal lesions. In this case there can be no doubt of the existence of a right-sided hemiplegia, and there is evidence that the left pyramidal tract has suffered too, in the indefinite type of the plantar reflex on this side. The tonic state of the muscles on the right side of the body, the "lead-pipe rigidity" of the limbs, and the persistent maintenance of postures, differs from that seen in both paralysis agitans and post-encephalitic lesions. The rigidity suggests that it might be the result of a combined hemiplegic hypertonicity and Parkinsonian rigidity. The postures of both the upper and lower limbs are not those usually observed in simple lesions of the pyramidal system. He emphasized the remarkable feature that the patient can open her hand only on supinating the arm, and that the whole limb extends when she closes her fingers. Similarly in advancing the leg the whole limb extends, and the ankle dorsiflexes only a considerable time later.

The PRESIDENT asked whether the present symptoms were the immediate sequel to the attack of encephalitis, or whether they had been progressive.

Dr. MCALPINE replying said that there was no interval between the acute symptoms of encephalitis and the symptoms which the patient now presents; these have been progressive. He was unable to accept Dr. Riddoch's suggestion that the hypertonicity is due to the association of a hemiplegic and Parkinsonian rigidity.

(3) *A Form of Juvenile Amaurotic Idiocy.*

By Dr. GEORGE RIDDOCH.

The patient, aged 10, was the child of Jewish parents, who were also first cousins. A brother aged 13, and a sister aged 8, are both alive and well. Birth was normal and the child was breast-fed until 18 months of age. He walked at 9 months and used simple words at 1 year. Development was normal until 4 years of age when the legs became weak. At 6 the upper limbs were also affected and obvious symptoms of mental deterioration set in, the child becoming dull and apathetic, with occasional outbursts of screaming and destructiveness. At the age of 8 years vision was noticed to be affected, and a year later there was complete paralysis of all limbs, curious myoclonic movements, over-reaction to loud noises, blindness and complete idiocy. The child also became subject to epileptiform fits. Any loud noise was liable to evoke irregular purposeless movements. The child has wasted considerably.

Present condition.—Complete dementia, blindness and spastic paralysis of upper limbs in flexion and lower limbs in extension. Lies on his back with head to one side and saliva dribbling from his open mouth. Quick involuntary movements, especially of upper limbs, occur frequently. These myoclonic movements can be evoked by the slightest tap on any part of the body, and sometimes by a loud noise. They are often bilateral and symmetrical and are then accompanied by movements of the head and face, contraction of the muscles of the trunk and a grunting noise. All tendon reflexes are much increased and the plantar response is extensor on both sides.

Ophthalmoscopic examination reveals advanced optic atrophy and much pigmentary degeneration of the retina; there is a large mass of pigmentary change near the left macula. No cherry-red spot at the macula. The Wassermann reaction of the blood was reported as being doubtfully positive.

He discussed the relation of this case to the Waren Tay-Sachs type of amaurotic family idiocy, which is limited to the Jewish race, and to the juvenile forms of this disease which have been described by Batten and Mayou and by others.

The PRESIDENT said he had found it difficult to get a satisfactory view of the fundi, but that such changes as he had seen resembled those of retinitis pigmentosa.

Dr. GORDON HOLMES pointed out that this case differs in many of its present symptoms from the typical cases of infantile and of juvenile amaurotic idiocy. The term idiocy should not, in fact, be applied to such cases, since the mental state of the patient was apparently normal till 5 or 6 years of age. The most striking difference from the Spielmeyer and Batten-Mayou groups is that in this patient there are, in addition to optic and retinal atrophy, large irregular patches of pigment in the retinæ which resemble those due to syphilitic retino-choroiditis. He was consequently not surprised that on one occasion the Wassermann reaction was positive or doubtful. Further, the pigmentary changes are grosser and more widely scattered over the fundus than in the Batten-Mayou group. In many of these cases the retinal degeneration belongs to, or resembles, the retinitis pigmentosa type, but the fundus changes he saw were not characteristic of this condition. There were unquestionably many forms of progressive dementia and paralysis associated with retinal degeneration, each rigidly typical for the several numbers of the family it affects, but differing in many respects from family to family.

Dr. PARKES WEBER suggested the possibility that the condition was one of juvenile general paralysis; the same type of spasmodic movements is not uncommon in this disease, and similar fundus changes are occasionally met with.

Dr. FEILING had also observed similar ocular changes in syphilitic conditions; he had recently seen them in a patient with tabes dorsalis.

Dr. RIDDOCH in replying admitted that the symptoms differed in many respects from those seen in the Batten-Mayou and Spielmeyer groups, and he must admit that similar retinal changes are found in both retinitis pigmentosa and in syphilitic conditions, but he could not see any justification for the suggestion that his case may be merely one of juvenile general paralysis.

(4) *A Specimen showing Endothelioma Cerebri in an Unusual Situation.*

By Dr. J. P. MARTIN.

Patient was admitted to the National Hospital under the care of Dr. Taylor, April 18, 1922, and died May 20. For three years he suffered with pins and needles in the third, fourth and fifth fingers of the left hand; this feeling was not present constantly and usually occurred in the morning. It spread slowly up the left arm, and he became unable to grasp objects with the left hand. Towards the end of 1920 the right arm was affected in the same way, but in it the paræsthesiæ spread from above downwards.

In January, 1921, he was admitted to St. Thomas's Hospital; his legs had been shaky but were still strong and did not cause any disability in walking; after lying in bed for four days he became completely paralysed. He gradually improved and was discharged three months later.

About July, 1921, he began to suffer from attacks of breathlessness. He was re-admitted to hospital, and again became weaker while lying in bed. About October, 1921, he became unable to feed himself or to use his arms. He never had dysuria or pain. On about a dozen occasions in three months before his admission to the National Hospital he had seen double.

On admission very helpless, with cyanosis of face and lips, and occasional attacks of breathlessness. A few nystagmoid jerks developed on extreme deviation of the eyes to either side, and there was slight left facial weakness.

There was nowhere loss to painful, tactile or thermal stimuli, but the appreciation of vibration was absent in both arms and both legs. The sense of position was lost in the right hand and arm and in both feet, and impaired in the left hand. There was complete astereognosis.

Patient could not raise his head from the pillow, but could turn it from side to side. When he was sitting in a chair his head fell forwards. Both upper limbs were quite powerless, they lay slightly flexed at the elbows and wrists, with the fingers half flexed. There was no spasticity and no wasting or fibrillation of the muscles. The lower limbs lay at rest in full extension. The amount of power varied from time to time: after he had been lying down he was usually unable to make any movement, but after sitting up for a time he could make movements of fair power at all joints.

All the arm-jerks were brisk, the knee-jerks exaggerated, ankle-jerks present with clonus, the abdominal reflexes absent, and the plantar responses both extensor. There was defective control over both anal and vesical sphincters.

The Wassermann reaction was negative, and the electrical reactions of the muscles were normal. X-rays showed no spinal lesion.

Patient died of hypostatic pneumonia.

Autopsy.—The tumour, which weighs 32·5 grm., is pear-shaped and firm in consistence. It fills and distends the cisterna magna, lying between the arachnoid and the pia mater. A small knob on its upper and posterior surface compresses the right lobe of the cerebellum. It lies against the foramen of Magendie, but has caused little hydrocephalus as the foramina of Luschka are unusually wide. The posterior surface of the medulla, from the tip of the calamus scriptorius downwards, is hollowed out by its pressure. The pressure affects particularly the cuneate and gracile nuclei, the restiform bodies being only compressed at their posterior borders. At the lower end of the medulla the tumour passes to the right of the mid-line so that the right dorso-lateral surface of the first cervical segment is compressed. The cord at this level is softened. Microscopical sections show the tumour to be a typical fibrous meningeal endothelioma.

(5) *Case of Sclerodermia.*

By Dr. MARTIN.

In March 1921, patient had an illness said to be influenza. In May she had difficulty in kneeling on account of pain in the thighs and back. In November she began to experience stiffness after standing for a short time. Menstrual periods have been irregular since January 1921. She has become thinner; a year and a half ago she weighed 8 st., now she weighs a little over 6 st.

Present condition.—High complexion, skin and subcutaneous tissues of the cheeks feel tough, skin of the nose red and shiny, lips puckered, mouth can be opened to a limited extent only. Scarcity of fat all over the body. The skin of the hands is hard, shiny and difficult to pinch up; the fingers are short, podgy and swollen, and cyanosed at the proximal phalangeal joints; their movements are limited and in the little fingers there are flexor contractures. The feet are flat, the joints are swollen and the toes and forepart of each foot are cyanosed. The elbows cannot be fully extended, the knees are prominent and rounded, and full extension is not possible at them.

No changes are present in the nervous, circulatory or respiratory systems.

(6) *A Case of Dermatomyositis.*

By Dr. MARTIN.

The symptoms had commenced gradually one and a half years before with pains in the limbs and swelling in the hands and feet. There had been no rise of temperature during the time the patient had been under observation. The most striking feature was the marked hardening of the skin and the subcutaneous tissues, and the presence of firm nodules scattered irregularly over the limbs; one of these was excised. At this operation there was found to be a marked thickening of the subcutaneous tissues. The nodule consisted merely of a fatty centre surrounded by a capsule of dense fibrous tissue, in which there were numerous inflammatory cells. In this case the limbs only were affected.

Dr. PARKES WEBER, in discussing the second case, pointed out that dermatomyositis is an acute inflammatory lesion of the muscles which has been frequently confused with trichinosis in countries where this disease exists. On examining this case he found no evidence of an inflammatory lesion of the muscles, while it appeared to him that the nodules were merely circumscribed lipomata. The condition is therefore not a dermato-myositis, but an affection closely allied to sclerodermia.

The first case seems to be one of typical generalized sclerodermia. It was interesting that so much improvement had been noticed, and he inquired as to the treatment which had been adopted.

The PRESIDENT drew attention to the curious course run by some of these cases, and to the fact that the muscles are sometimes involved. He recalled a case of acute sclerodermia, from the manifestations of which the patient had made a complete recovery, but then developed typical symptoms of progressive muscular atrophy.

Dr. MARTIN in replying stated that the second case had been treated by thyroid extract, sinusoidal current baths and massage during the past three months, and that it was under this treatment that some degree of recovery had taken place.

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CLINICAL MEETING AT THE NATIONAL HOSPITAL FOR THE PARALYSED AND EPILEPTIC, QUEEN SQUARE, W.C., ON THURSDAY, JANUARY 11.

Dr. WILFRED HARRIS, President, in the Chair.

(1) *Case of Dystrophia Myotonica.*

By Dr. W. J. ADIE.

W. A., aged 44. Married. Enjoyed good health until March, 1917, when whilst undergoing military training he passed through a severe feverish illness diagnosed as influenza; during convalescence he suffered from severe pains in the lower limbs; the pains subsided in a few months but left behind them a weakness of the lower limbs which steadily increased, and soon appeared in the arms as well. About a year after the onset of weakness in the legs, and some time after the arms became weak, he noticed that he had difficulty in relaxing his grasp; this trouble persists. His facial appearance has altered considerably; all his muscles have wasted; his speech is not so clear as it used to be; his hair is falling out rapidly; he has lost over 2 st. in weight; he has not had sexual connection for some years and desire is absent. Apart from weakness in the limbs he feels well. He has never heard of a similar complaint or of cataract in any other member of his family. He has four healthy children.

Present condition: Facies myopathica; atrophy of sternomastoids, deep neck muscles, forearms and legs. Active myotonia in hand grasps. Reactive myotonia in tongue, small muscles of hands, deltoids and thighs. All tendon reflexes absent. Frontal baldness, acro-cyanosis, small soft testicles, narrow, high-arched palate.

(2) *Case* of *Myotonia Congenita.*

By Dr. LEWIS R. YEALLAND.

P. S., aged 18, male; one of twins. A paternal uncle suffers from cataract; nothing else from an hereditary point of view is discoverable. The patient was breast-fed and there was no difficulty in feeding him. He began to walk at the age of 2 years (a year later than his twin brother), was clumsy and made slow progress. At the age of 2½ his mother first noticed that when the patient's face was slapped for punishment, "his nose drew over to one side and remained there for a few seconds." At the age of 3, the patient was taken to India with his parents, and during his five years there nothing abnormal was observed; he walked normally and played games with other children. At the age of 8, he returned to England and began school. During his first week there (*a*) he saw double when looking at the blackboard from an angle; (*b*) his hand became "stiff" when writing and he was unable to release his pencil from it; (*c*) at the first school drill he was compelled to fall out after twenty minutes' participation, on account of a gradually increasing stiffness which began in the neck and spread rapidly to the arms, trunk and legs. The stiffness was superseded by limpness, and in less than thirty seconds from the commencement of the symptoms he fell and was unable to move. He was taken home and remained in bed three days limp and helpless, but was able to swallow his food when fed. Similar attacks have occurred since during exertion, and an attack will come on after thirty minutes to one hour's walk in the cold. In warm weather he is almost free from the attacks. After prolonged rest the patient is much better, and he is in his best state the first thing in the morning after a prolonged rest. The condition is gradually becoming worse.

The patient is well developed. There are no deformities. Skin, mucous membrane, skull and spine, heart and lungs are all normal. The optic discs are clear and there are no evidences of organic changes in the central nervous system.

Repetition of any voluntary movement to order (e.g., eye movements, whistling, biting, yawning, flexion and extension of the elbow, wrist, knee or ankle) produces a gradually increasing tonic contraction of the part and will, if persevered in, result in complete cessation of movement. The same state of stiffness can be induced by the patient at will by throwing groups of muscles forcibly into contraction. Relaxation of muscles occurs gradually and is independent of the patient's will. Relaxation of the hand grasp is slow and awkward, the index finger extends first, followed by the others in succession, and the movement seems to be dependent on the patient's effort. A slow tonic contraction of muscles follows a sharp tap of the percussion hammer. The myotonic electrical reactions are positive.

DISCUSSION.

Dr. JAMES COLLIER considered that there was no doubt about the diagnosis of myotonia congenita in this case. It showed in a typical manner the effect of cold in increasing the tendency to myotonia, and resembled most reported cases in that the spasms were not decreased by exercise of the affected muscles.

The PRESIDENT asked Dr. Yealland if he had seen attacks in which the patient was helpless. Was it possible that these attacks were in any way similar to attacks of family periodic paralysis ?

Dr. YEALLAND replied that he had not himself observed such attacks, but the evidence he had been able to collect tended against this suggestion.

(3, 4, 5) *Three Cases showing Retraction of the Eyelids.*

By Dr. JAMES COLLIER.

(3) *Case of Tumour affecting the Mid-Brain.*

The patient presents the following signs: Pronounced psychic impairment. Papillœdema. The pupils react very poorly to light, often the right pupil does not react to light at all. Retraction of both upper eyelids. Defective upward movement of the eyes. Right facial weakness, especially on emotional movement. Absolute incontinence of urine. Slight weakness of the right side of the body, with extensor plantar reflex on that side.

(4) *Case of Mid-Brain Lesion.*

A. K. History: In October, 1921, the patient noticed shaking of the right hand; it passed off after about a fortnight. In February, 1922, the tremor returned: both the right arm and the right leg began to shake and she had double vision; her speech became slow and jerky.

Examination: Discs clear. Nystagmus: Vertical in right eye, oblique in left. Defective upper movement of both eyes; left eye turned slightly downwards and inwards. Ptosis of right upper lid; retraction of left upper lid with positive von Graefe's sign. Speech very ataxic. During speech there is a rhythmical upward and downward movement of the eyebrows and tremor of the head. There is a coarse tremor of the right hand. No loss of power in the limbs. No changes in the reflexes, except that the plantar reflex on the left side is doubtful.

(5) *Case of Disseminated Sclerosis with Retraction of the Eyelids.*

G. L., aged 41. Right leg began to drag seven years ago; since then symptoms have been steadily progressive, and consist of stiffness in both legs, spasms of lower limbs at night, precipitancy of micturition and incontinence.

Examination: Pupils equal; react normally. Nystagmus. Retracted lids, von Graefe's sign present. Slight intention tremor in hands; no ataxy or loss of power of upper limbs. Lower limbs very spastic, frequent flexion spasms.

Reflexes: Arm jerks all present; knee and ankle jerks exaggerated. Abdominal reflexes absent, plantar reflexes both extensor. Cerebrospinal fluid shows no abnormality.

(6) *Case of "Spondylose rhizomélique."*

By Dr. JAMES COLLIER.

The vertebral column is rigidly ankylosed throughout its length; the hip joints and knee-joints are also immobile; the right shoulder-joint shows great limitation of movement. The disease began ten years ago; patient has been in a spinal carriage for five years.

X-rays showed ossification of the short intervertebral ligaments.

DISCUSSION.

Dr. J. G. GREENFIELD asked whether there was in this case any sign of gonorrhœa, or of any focus of chronic sepsis. Some cases of this affection had been attributed by French writers to gonorrhœa. He remembered a case under Dr. Batten's care in the National Hospital in 1911,[1] in which gonorrhœa was suspected but could not be proved. In the majority of cases the disease commenced about the age of 20, and this fact, as well as the nature of the pathological changes and the distribution of the ankylosis (which always left the hands unaffected) distinguished spondylose rhizomélique from the chronic rheumatic diseases of the spine.

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[1] Case shown at Meeting of Neurological Section of the Royal Society of Medicine, May 4, 1911.

Dr. COLLIER replied that of six cases of this condition which he had observed none had suffered from gonorrhœa, nor was there any history or evidence of it in the present case. In one of his cases the disease came on after puerperal sepsis, but in the others there was no focus of infection. In the majority of his cases the spine had been ventrally curved, but in one it was curved backwards as in the present case. In one case the affection started in the neck, and in six months spread down the spine to the sacrum rendering the patient as helpless as if he had developed total paraplegia. He considered that the ankylosis of the spine was never bony as there was always pain on any attempts at passive movement.

(7) *Case of Disseminated Sclerosis with Muscular Wasting.*

By Dr. JAMES TAYLOR, C.B.E.

H. C., aged 47. Previous health good. Fracture of left leg below knee when aged 13. Present trouble started eight years ago by the left knee giving way and the left leg becoming weak. One year ago he discovered that on reading he "was using the left eye only." About the same date the left grasp became weak and a sensation of pins and needles was felt in the left forearm and hand. There was also dysuria.

On admission, November 6, 1922: Vision of right eye $\frac{6}{18}$, of left $\frac{6}{60}$. Left disc distinctly pale, chiefly in temporal half. Nystagmus on lateral deviation to both sides. Marked spasticity of left upper and lower extremities. Wasting of left trapezius and muscles of left shoulder-girdle. Weakness of right rhomboids. The left arm and leg are less bulky and thinner than the right. Subjective sensation of pins and needles in left forearm and hand, and numb feeling in the feet. Slight diminution to cotton wool and pin-prick over left leg. Extensors wasted. Plantars, right extensor, left flexor. Left ankle clonus. Knee and ankle jerks increased. Abdominals absent left, doubtful right. Wassermann reaction negative in blood and cerebrospinal fluid. X-ray examination shows lipping and osteophytic outgrowths of cervical and lumbar vertebræ.

The evidence of disseminated sclerosis in this case rested chiefly on the nystagmus, the difficulty in articulation and the signs of lateral sclerosis. The winging of the scapulæ was probably due to some other cause, and it was possible that the osteophytic growths in the spine might account for this and some of the other symptoms.

Discussion.

Dr. COLLIER said that he would never admit wasting of muscles as a symptom of disseminated sclerosis.

The PRESIDENT said that he had seen quite definite atrophy of the interosseous muscles of the hands in disseminated sclerosis.

(8) *Case for Diagnosis: Spinal Compression or Disseminated Sclerosis.*

By Dr. F. M. R. WALSHE.

E. W., aged 37. Past health good. Patient has six children, all in good health. Duration of symptoms eighteen months. Onset with pain in sole of left foot, followed by stiffness at back of left knee. In three months time lost the use of left leg. Sensation of pins and needles in left leg when it was accidentally bumped. The right leg became weak and powerless two months later. Dysuria for the last six months.

On examination, December 27, 1922: No abnormality of the cranial nerves or upper extremities. Legs usually in rigid extension, feet plantar flexed, halluces in extension. Marked adductor spasm. Flexor spasms of the legs have been becoming more frequent. No sensory changes. Knee and ankle jerks increased. Plantars give extensor responses. Abdominal reflexes: Upper feeble, lower absent. Reflex responses to cutaneous stimulation of both legs very active. Cerebrospinal fluid clear, colourless, no cells; total proteid 0·1 per cent. Wassermann reaction negative in blood and cerebrospinal fluid.

DISCUSSION.

Mr. C. P. SYMONDS said that he had never seen a case of disseminated sclerosis in which the protein in the cerebrospinal fluid rose as high as 0·1 per cent.

(9) *Case of Syringomyelia.*

By Dr. S. A. KINNIER WILSON.

L. H., aged 16. Previous health: Diphtheria, "rheumatism" at the age of 4, and frequently since in legs, arms, and shoulders. Operation for adenoids when 10 years old. Twelve months' history of painless sores on the right hand and fingers.

November 12, 1922: Experienced a feeling of coldness in right half of body. At the same time she noticed that she could not appreciate the temperature of water with the right arm or hand. At the same period she noticed the left pupil was getting smaller and the left eyelid drooping.

On admission, December, 1922: Left pupil smaller than right, left eyelid drooping. Slight impairment of tactile sensibility, marked thermal and pain loss in left trigeminal area. Tongue on protrusion deviates slightly to the left. Very slight spasticity of right arm and leg. Right leg weaker than left. Sensory loss to pinprick and temperature over right half of body up to a transverse line in mid-cervical region. Faint diminution to tactile stimuli over the same area. Knee and anklejerks greater on right than on left side. Plantars: right doubtful, left flexor. Sphincters unaffected.

(10) *Case for Diagnosis, possibly Amyotonia Congenita.*

By Dr. S. A. KINNIER WILSON.

B. W., aged 11. Child born normally. Began to walk at normal age. He is the second youngest of eight children. At the age of 4 he was noticed by his mother to be double-jointed. He began at this time to "fall about." The weakness of the legs has been progressive in the last three years. At present he is unable to stand unsupported.

Mentally the child is bright and intelligent. When sitting up the back is unduly rounded. The arms are thin and their strength poor. The muscular power of the legs is very poor. Impaired muscle tone in all limbs, the deficiency being greater in the legs than in the arms, over-extension at the knees on passive movements being very prominent. No contractures present. Arm-jerks very feeble. Abdominals active. Knee-jerks: Right greater than left, which is feeble. Ankle-jerks: Right feeble, left not obtained. Plantars: Right indefinite, left flexor. Sphincters unaffected.

(11, 12) *Congenital Neurosyphilis in Brother and Sister.*

By Dr. S. A. KINNIER WILSON.

(11) D. J., aged 10. Epileptiform fits since age of 5. Automatism, spitefulness. Mentally clear, Hutchinson's teeth. Pupils unequal, poor light reaction. Wassermann in blood, negative.

(12) G. J., aged 7. At the age of 5, paraplegia; unable to walk since arrest of mental development. Pupils Argyll-Robertson. Knee-jerks increased, plantars extensor, gait spastic and stamping. Ocular fundi, disseminated choroiditis. Wassermann in blood positive.

DISCUSSION.

Dr. JAMES TAYLOR said that in his experience two members of a family with congenital syphilis usually suffered in different ways. One of his patients, a boy who was afflicted with optic atrophy, was brought to hospital by a younger sister who had Hutchinsonian teeth, interstitial keratitis, and other signs of congenital syphilis, which were absent in the brother. The older patient eventually developed G.P.I. and died, whereas his sister remained free from symptoms of nervous disease.

The PRESIDENT said that Dr. Taylor's cases argued strongly against the assumption that there was a neurotoxic strain of the *Spirochæte pallida.*

(13) *Case of Syringomyelia, with much Sensory and Motor Impairment and little Wasting.*

By Dr. C. M. HINDS HOWELL.

M. G., aged 23. Patient "fell down" in a seizure or faint while at work in February, 1919. Afterwards she had an illness thought to be influenza. After the illness she was troubled with "hot sweats" affecting the left shoulder and left side of neck and head. Later she noticed weakness of the left hand while at work. In February, 1922, the right leg began to feel stiff and she had a sensation of cold waves passing up and down this limb.

On examination it is found that the left pupil is greater and the left palpebral fissure smaller than on the right side. There is no nystagmus. There is partial loss of pain sense and of appreciation of cold over the left half of the forehead and over the lateral part of the left cheek. The left arm is weak, particularly the hand grasp; the thenar and hypothenar eminences are wasted. The deep reflexes are absent in the left arm. The right arm shows no weakness or wasting.

Both lower limbs are spastic, right more so than the left. The knee and ankle jerks are exaggerated and ankle clonus is present. Both plantar reflexes are extensor.

There is loss of tactile sensibility over the outer side of the right leg only. Pain sense is lost over both arms and both shoulders, and is impaired all down the right side of the trunk and over the whole of the right lower limb; on the left side of the body there is a similar impairment down to the lower border of the fourth dorsal segment both in front and behind.

Recognition of heat is completely lost over the whole of the right half of the body except the face, and over the left arm and left side of the trunk down to the level of the tenth dorsal segment. Loss of recognition of cold corresponds almost exactly in its distribution to the impairment of sensibility to pain.

(14) *Case for Diagnosis.*

By Dr. C. M. HINDS HOWELL.

G. S. In October, 1922, eight weeks before admission to hospital, patient's legs became weak while he was out walking; for about a week before that he had been losing the grip in the left hand and the left arm used to hang limply. Since the day when his legs gave way he has become steadily weaker and he has been aware of flickering in the muscles of his thighs. Since admission the right arm has become weak and he has become incontinent of urine and fæces. His neck has become stiff and it is painful when moved.

Examination: Left pupil slightly smaller than right. Fibrillation present in tongue. Complete flaccid palsy of left arm. Right arm becoming rapidly weaker. Abdominal and chest muscles weak; diaphragm does not seem to be acting. Left lower limb weaker than right. Fibrillation in muscles nearly all over the body, but especially in the thighs; wasting most pronounced in the muscles of the back and in the left lower limb. Sensory loss variable; fairly complete in both arms, less complete on chest with a level at the angle of the sternum. Sensory loss on the lower limbs much less than on the upper; right lower limb more affected than left. Reflexes: Knee-jerks brisk; plantars extensor.

Most of the signs presented by this case suggested the diagnosis of compression of the cervical region of the cord by a tumour. But this would not explain the fibrillation which was present. X-rays showed erosion of the second cervical vertebra and some shadows suggesting an intrathoracic tumour. As the condition was rapidly progressive he considered that it was probably due to a diffuse sarcomatous or gliomatous invasion of the spinal cord. The cerebrospinal fluid contained 0·1 per cent. protein.

DISCUSSION.

The PRESIDENT described a somewhat similar case with total paralysis and anæsthesia of the right arm and partial paraplegia in which he had advised operation. The surgeon found no tumour, but noted no pulsations of the cord or dura mater. He therefore explored upwards under the laminal arches and came against a resistant mass. When he tried to break through this there was a gush of blood which proved, post mortem, to have come from an aneurysm of the posterior inferior cerebellar artery.

Dr. JAMES TAYLOR said that he had seen a similar case, which also presented the symptom of fibrillation of muscles, and which proved to be due to gliomatosis of the cord.

Dr. RIDDOCH described a case of quadriplegia with signs of spinal compression and multiple root lesions but with few sensory alterations, due to sarcomatosis of the meninges. The cerebrospinal fluid in this case was yellow, very highly albuminous and contained many tumour cells, some of which showed mitotic figures.

(15) *Case of Disseminated Sclerosis.*

By Dr. W. ALDREN TURNER.

G. W., aged 35. About one and a half years ago patient began to be troubled with a trembling of the right arm, becoming more marked when he used the arm; this tremor has gradually become coarser. About the time the tremor commenced patient's gait became somewhat unsteady. Fifteen months ago his speech became jerky and has got steadily worse up to the present. Four years ago patient fell off a bicycle, striking his head and bruising his right elbow.

Examination: Discs normal. Pupils unequal, left greater than right, regular, slightly eccentric, some retraction of eyelids, react normally. External ocular movements good, no nystagmus, squint or diplopia. Movements of face, palate and tongue normal. Numbness in both hands. No demonstrable loss to pinprick or cotton wool. Sense of position in space and localization of touch normal. No astereognosis. Violent intention tremor of the right arm, so great that it shakes the whole body. The tremor is not purely intentional, for it is sometimes present mildly in the shoulder during rest. The left arm shows a slight tremor of the intention type. There is no loss of power or limitation of movement. Arm-jerks: equal on the two sides; biceps-jerk not obtained. Right knee and ankle jerks greater than left. No ankle clonus. Abdominals: present and equal on the two sides. Plantars: both flexor. Gross ataxia of gait: the arms, especially the right, make large movements which react on the whole body. No Rombergism. Wassermann reaction negative. The cerebrospinal fluid is normal except that it gives a "paretic" curve with the Lange test.

Progress: Little change noticed in arms, though patient feels that the tremor of the right arm now involves the shoulder more. Both legs are affected by tremor and the left is now rather worse than the right.

DISCUSSION.

Dr. SYMONDS said that he had noticed in the history of this case that the patient had had an illness called "influenza" six months before the onset of the tremor. He considered it possible that this was really a mild attack of encephalitis lethargica. He had seen involuntary movements follow an attack of encephalitis lethargica so mild as not to keep the patient in bed. He had observed Lange reactions of the "paretic" type in the cerebrospinal fluid of two cases of encephalitis lethargica.

Dr. RIDDOCH was inclined to agree with Dr. Symonds in considering that this case was due to encephalitis lethargica. The steady onset of symptoms without any remission was unlike disseminated sclerosis. He had often noticed similar gross involuntary movements come on gradually after encephalitis lethargica.

(16) *Case of Unilateral Affection of the* 7, 9, 10, 11, *and* 12 *Cranial Nerves.*

By Dr. C. P. SYMONDS.

Miss T., aged 30. In July, 1919, she had some teeth extracted. Shortly afterwards she noticed a discharge from her left ear, for which she did not consult a doctor. This was followed by gradually increasing deafness in the left ear. In March, 1920, she first noticed hoarseness which prevented her singing. About the same time she began to experience pain in the left shoulder and found that this occurred especially when she attempted to carry heavy objects in the left hand. In the summer of 1921 her voice improved, so that she was again able to recite, though singing was still impossible. The pain in the left shoulder was also less noticeable. During the last year the voice has again become hoarser, and the trouble in carrying things with the left arm has increased. She has also occasionally noticed some difficulty in swallowing. In October, 1922, for the first time she had a brief attack of left facial spasm. In this the eye closed and the whole side of the face was screwed up. Since then she has had several such attacks.

On examination the positive findings are: Left-sided conduction deafness, together with a fleshy mass obscuring the membrana tympani, probably a polyp. A fragment has been removed for microscopical examination, which shows it to be a capillary angeioma. Left facial palsy of peripheral type. Paresis of the left vocal cord and left side of the palate. Weakness and wasting of the left sternomastoid and trapezius. Atrophic palsy of the left side of the tongue. Wassermann negative in blood. X-ray of head and upper cervical spine negative.

(17) *Case of Unilateral Affection of Cranial Nerves* 9 *to* 12 (*Tapia's Syndrome*) *associated with Chronic Otitis Media.*

By Dr. C. P. SYMONDS.

Miss C., aged 35. She has suffered from bilateral otorrhœa from time to time since childhood. She had tonsillitis at the age of 28, is subject to headaches, and has attended Guy's Hospital for constipation. In February, 1921, she first noticed hoarseness, and was referred from the medical to the throat department. It was there observed that the left vocal cord was paralysed. When seen a few days later the positive findings were: Paralysis of left vocal cord and weakness of left side of soft palate. Weakness and wasting of left sternomastoid and trapezius. Atrophic palsy of the left half of the tongue. Evidence of old-standing otitis media on both sides with a moderate degree of conduction deafness. The blood: Wassermann was negative. X-ray of the head and of the upper cervical spine showed no abnormality.

Under observation this patient has shown little change during the past two years except for the tendency of the hoarseness to diminish.

DISCUSSION (Cases 16 and 17).

The PRESIDENT considered Dr. Symonds's cases to be similar to those described in textbooks as "polyneuritis cranialis," the causation of which had been traced in some cases to otitis media.

Dr. COLLIER said that he had followed seven similar cases to autopsy, and in every case osteomyelitis of the base of the skull had been found. In one the disease had followed a bullet wound of the cranium; in another a tubercular osteomyelitis of the basi-sphenoid, and in the remainder ear disease was the cause. The appearance seen in the posterior fossa at autopsy was a plum-coloured cushion of raised and thickened dura mater with disintegration of the underlying bone. In every case the causative organism was a streptococcus. The long duration and the absence of pyrexia were remarkable. In one case there was no clinical evidence of otitis media, although the autopsy proved that this had existed. He placed no reliance on X-ray evidence in this condition, as it was very difficult to get satisfactory radiograms of the posterior cranial fossa. The cause of death in his cases had been lepto-meningitis in every case except the tubercular one, in which the carotid artery was eroded, and burst into the pharynx. One case had developed a hemiplegia, which was found to be due to thrombosis of the superficial veins of the brain. Replying to a question by Dr. SYMONDS whether the operative findings in Case 16 were not against his conception of the disease, Dr. COLLIER replied that in two cases following ear disease autopsy showed that the mastoid region was healthy, but that the infection had spread through the apex of the petrous bone.

NOTICES OF RECENT PUBLICATIONS.

Nerve Exhaustion. By MAURICE CRAIG, C.B.E., M.D., F.R.C.P. Pp. 148. London: Churchill. 1922.

This small volume is intended as a guide to the treatment of nervous exhaustion, under which term the author includes a large number of morbid conditions, arising from many different causes; these are considered in detail. He treats very shortly of emotional shock, over-work, worry, and touches on physical states, such as puerperium and lactation, which lead to exhaustion. These various symptoms are attributed for the most part to "hypersensitivity," congenital or acquired, on which the author lays great stress. A chapter is devoted to sleeplessness, and the final section to treatment in general. The book is intended for the general practitioner, who is anxious to learn in simple language the means at his disposal for dealing with this aspect of the functional psychoneuroses.

Etudes Neurologiques. By GEORGES GUILLAIN. Pp. 469. Paris: Masson et Cie. 1922. Price 25 francs.

The author has reprinted in this volume all those earlier papers in which he has brought forward any new facts related to the symptomatology and pathogenesis of nervous disorders. He has arranged them, not in chronological order, but in separate chapters according to the main subject with which they are concerned. The titles of these chapters reveal his wide interest and the valuable work he has done; the most important are: The fixation of poisons in the nervous system, pathology of the brain, pathology of the spinal cord, syphilis of the nervous system and tabes, muscular atrophies, changes in the cerebrospinal fluid, lethargic encephalitis and intoxications.

Many of the papers included are, it is true, only short communications originally published in various medical journals, and some perhaps are no longer of great interest or importance. But several of them at least have a real value, and the majority are certainly worth collecting together in a more permanent and easily accessible form. This is largely due to the fact that Guillain's interests have been mainly in the pathological and anatomical aspects of disease, and that his conclusions, as well as his hypotheses when he ventures on such, are solidly based on direct evidence of structural change. In fact in his introduction to this volume he insists that the anatomy and physiology of the nervous system must be the basis of any advance in knowledge which we can hope to attain, and that in the study of neuropathology all the modern methods of biology, bacteriology, chemistry and physics must be applied. A worker who has been guided by these principles must almost necessarily have valuable results to offer his readers.

Multiple Sclerosis (Disseminated Sclerosis): An Investigation by the Association for Research in Nervous and Mental Diseases. Pp. 241. New York: Hoeber, 1922.

The Second Annual Meeting of the American Association for Research in Nervous and Mental Diseases, which was held in New York in December, 1921, was devoted to a discussion on the etiology, pathology, symptomatology, differential diagnosis and treatment of disseminated sclerosis. The proceedings and conclusions of the commission are recorded in this volume, which constitutes a valuable contribution to our knowledge of this disease.

All the possible factors in the pathogenesis of the disease are discussed; several pages are even devoted to the hypothesis put forward by Jelliffe that as unconscious emotional factors are known to be under greater tension and more constantly operative than conscious ones which can produce somatic alterations, they may excite exudate phenomena in the blood-vessels of the nervous pathways intimately related to the function under repression, and therefore produce the characteristic lesions of disseminated sclerosis. But most of the papers and discussions are distinguished by a practical common sense. The sections on the vestibular and ocular manifestations of the disease are particularly interesting, and the negative results of Teague's prolonged research on its possible bacterial or protozoal origin are important in view of the recent repeated discoveries of causal micro-organisms. The chapters on the pathology of multiple sclerosis and on the changes that occur in the axis-cylinders are particularly complete.

The volume ends with a very comprehensive bibliography which, together with the statistical information collected in it, will prove extremely useful to all who wish to study the disease.

Der extrapyramidale Symptomenkomplex (das dystonische Syndrom) und seine Bedeutung in der Neurologie. By Professor G. STERTZ. S. 96. Berlin: S. Karger, 1921. Price 18 Marks.

This small monograph is devoted to those affections of the nervous system the most pronounced characteristics of which are disturbances in the functions of the motor system, and especially abnormalities of tone, unassociated with symptoms of affection of the cortico-spinal system. The clinical conditions included are progressive lenticular degeneration, pseudosclerosis, paralysis agitans, double athetosis, torsion spasm, spastic athetosis, choreic movements and myoclonia. In the second section the relations of the functional disturbances produced by non-systemic diseases of the basal ganglia, as arterio-sclerosis, disseminated sclerosis, tumour, encephalitis and poisons are considered; and the final chapter is devoted to a careful analysis of the pathology and physiology of the so-called extra-pyramidal systems. This is probably the section which will excite most interest, as subjects claiming more and more importance in neurology are clearly and systematically dealt with in it. Unfortunately the author's style makes the reading of it difficult.

Beiträge zur Entwicklungsgeschichte des menschlichen Gehirns. Teil 2, Leiferung 1. *Die Entwicklung der Zirbeldrüse.* von Professor F. HOCHSTETTER. S. 45. Mit 6 Abbildungen im Text under 4 Tafeln. Wien und Leipzig: Deuticke, 1923. Price 10 Marks.

In this monograph, which is devoted to the development of the pineal gland in man and other mammals, Hochstetter has recommenced the issue of his valuable contributions to the embryology of the brain.

Certain features of disease of the pineal body have lately attracted considerable attention and consequently even to clinicians this monograph, in which many points on the origin and development of the gland are cleared up, offers some interest. It is, for instance, important that at one stage of growth the cells of its anterior lobe have an acinous or gland-like arrangement, suggesting a potential secretory function, which though not visible in the later stages of development may be reproduced in growths originating from these cells.

The plates by which the work is illustrated are extremely well reproduced, and make it possible to follow the descriptions of the text with ease.

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ON CERTAIN TONIC OR POSTURAL REFLEXES IN HEMIPLEGIA, WITH SPECIAL REFERENCE TO THE SO-CALLED "ASSOCIATED MOVEMENTS."[1]

BY F. M. R. WALSHE, M.D., F.R.C.P.

Neurologist in the Medical Unit, University College Hospital, and Assistant Physician to the National Hospital, Queen Square, London, W.C.

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[1] The expenses of this investigation were defrayed by the Graham Research Fund.

CHAPTER I.—INTRODUCTION.

IN earlier papers the writer has endeavoured to analyse in physiological terms the spasticity resulting from pyramidal system lesions and also the reflex movements in the lower limbs in the two clinical forms of paraplegia, the extended and the flexed [15] [16]. These phenomena were identified with certain tonic and phasic reflex reactions described by Sherrington. A similar detailed analysis of the familiar associated movements of the paralysed limbs in hemiplegia remains to be undertaken on the same lines. In the papers referred to above some preliminary considerations on the subject were stated. Thus, these movements were described as tonic or postural reactions, that is, as reflex variations in muscle tone, rather than as movements in the strict physiological sense. This conclusion was based upon the following considerations.

Neurologists are learning from Sherrington to regard muscle tone as the basis of posture, and decerebrate rigidity as a form of reflex standing. In the earlier analysis of spasticity, as it occurs in hemiplegia and in the extended form of spastic paraplegia, reasons were given for regarding it as physiologically identical with experimentally produced decerebrate rigidity. It was pointed out that all voluntary purposive movements are accompanied by an appropriate postural adjustment of the rest of the skeletal musculature, and that in forceful movements this adjustment or adaptation is necessarily bilateral and widespread. Although carried out under voluntary control, postural adaptation is a function of reflex mechanisms situated in the brain-stem, which are not put out of action by the lesion which produces hemiplegia and abolishes voluntary control of the musculature on the affected side of the body. In these circumstances, we should still expect postural reactions to occur when forceful voluntary motor activities are carried out by the musculature of the sound half of the body. Now, however, deprived of cortical control, they would occur in exaggerated intensity and deprived of that fineness of adaptation which that control ensures. It was concluded that the "associated movements" of hemiplegia are phenomena of this order, appearing in the muscles of the affected side on certain voluntary movements of the normal limbs, or on such semi-voluntary movements as yawning. In other words, associated movements, or, as we shall call them, "associated reactions," are released postural reactions in muscles deprived of voluntary control.

With certain modifications in detail, this view as to the nature of associated movements was reached by Riddoch and Buzzard [8]. The recent work of Magnus and his collaborators on the nervous regulation of posture in animals has indicated lines along which a further investigation may be carried out, and it is now proposed to record observations on such of the tonic reflexes described by Magnus as are to be found in man in cases of hemiplegia, and also to establish what relation, if any, there may be between these reflexes and the familiar associated reactions. Elsewhere [17] the present writer has given a résumé of the researches of Magnus and de Kleijn, to which the reader may be referred for more complete details than it is here possible to give. A short summary of the general nature and bearing of part of this work is, however, necessary at this point, so that the nomenclature adopted from time to time and the conclusions ultimately reached may be clear. In his experimental analysis of muscle tone, Sherrington showed that the tone of a given muscle is dependent upon the integrity of its afferent nerve supply. In addition, he observed that afferent impulses arising in the labyrinths and in the muscles and joints of the neck and limbs are capable of modifying, or of regulating, muscle tone. The researches of Magnus and his school have been devoted to the study of these regulating mechanisms and may now be said to have solved the main problems in the co-ordination of posture. Beginning with the decerebrate animal it was found that the otolith organs of the labyrinths (and not the semicircular canals) and the proprioceptors of the neck are the sources of impulses which by their influence on muscle tone produce reflexly a whole variety of attitudes of the limbs and trunk. Thus, changes in the position of the head (otoliths) in relation to the horizontal plane of space cause an identical variation in the extensor tonus of all four limbs. The maximal influence is exerted when the animal is inverted, and the minimal when the animal stands on its feet in a natural posture. Alterations in posture of the head in relation to the trunk also produce variations in limb tonus and therefore in attitude, quite apart from labyrinthine influences. Thus, rotation of the head to one side causes increase of extensor tonus in the limbs on the side to which the snout is directed, and diminution of extensor tone in the crossed limbs. Retraction of the head produces extensor spasm in the fore limbs and loss of extensor tone in the hind limbs, and ventral flexion of the head has the opposite result. In these circumstances the decerebrate animal can maintain a standing posture if it be carefully placed therein, and the variations in attitude described are not actively produced by reflex movements of the head, but by the observer who uses the head as a species of handle and thus sets up the postural reactions described. Apart from this the head of the decerebrate animal is unalterably retracted, and does not possess the capacity of righting itself in space. Clearly, therefore, some of the postural mechanisms present in the nervous system of the intact animal have been removed in the process of decerebration, in which the brain-stem has been transected between pons and mid-brain. The study of the "mid-brain" preparation, an animal in which transection has been performed immediately cephalad to the mid-brain, reveals the localization of the remainder of the posture-regulating mechanism, for this preparation can not only stand, but can walk, run and jump, and can right itself no matter in what abnormal attitude the observer may place it. The sum total of the postural reflexes active in the decerebrate animal Magnus [5] speaks of as "standing reflexes," while the additional reflex reactions present in the "mid-brain" preparation, which enable the animal to maintain full reflex control of posture, he speaks of as "position" or "righting" reflexes ("Stellreflexe"). He has analysed these into five groups, according to their source and the muscles upon which they act. In apes, these five groups are: (1) optic (probably retinal) righting reflexes; (2) labyrinthine righting reflexes acting upon the head; (3) righting reflexes arising in the deep tissues of the body wall and regulating the position of the head; (4) righting reflexes arising in the deep structure of the neck and acting upon the trunk and limb muscles; and (5) righting reflexes arising in the deep tissues of the body wall and acting upon limb and trunk muscles.

It will be noted that Magnus does not record the existence of tonic reflexes (either "righting" reflexes, or "standing" reflexes) arising in the limb muscles and joints and acting on the limb muscles, though, as we have mentioned, Sherrington has found evidence of such reactions. [9]. As will appear later, it is to such a group that the associated reactions belong. In speaking of tonic reflexes arising in the labyrinths, we refer particularly to the otolith organs in the utricle and saccule, and not to the semicircular canals which play no part in the production of the tonic reflexes now under consideration. Further, it will be seen that the term "Stellreflexe" is here translated as "righting reflexes." This is clearly not a literal translation, which has been avoided as not conveying the full significance of this variety of tonic reaction. In a communication received by the present writer, Magnus has expressed the opinion that the translation adopted most adequately conveys his interpretation of the reflexes in question.

CHAPTER II.—ASSOCIATED REACTIONS.

The so-called "associated movements" of hemiplegia which appear most characteristically in the limbs of the affected side are so familiar to neurologists that a detailed description of them is scarcely necessary. An admirable account of them has recently been given by Riddoch and Buzzard in a paper already referred to, in which these observers indicate how widespread these reactions may be, involving head, trunk and limb musculature. Such description of them as we shall give will be directed primarily to the elucidation of their nature and physiological significance, rather than to providing a general account.

The clinical material on which the present paper is based consists in the first place of a series of eighteen cases of hemiplegia studied during the years 1912-1914, when the reflex movements of the lower limbs were more particularly the object of study. The conclusions then reached have been briefly summarized in the introductory chapter, and have also been expressed in an earlier paper [16]. At that time the early papers of Magnus and de Kleijn were not accessible, and therefore no final analysis of associated reactions could well be carried out. Recently, however, a fresh series of twenty cases have been investigated and the whole subject re-surveyed in the light of our present knowledge of the nervous regulation of posture. Of the original series, five were cases of flaccid hemiplegia of recent origin, three due to vascular lesions in the region of the internal capsule, and two to cerebral compression by tumour. The present series consists of spastic hemiplegias with the usual signs of pyramidal tract involvement. This spasticity was of the familiar type, the arm being spastic in flexion and the leg in extension. In all but one the lesion was vascular in origin and presumably in the region of the internal capsule. The exception was a case of left-sided cerebral tumour, the exact localization of which yet awaits verification.

It may be observed that while we have compared the spasticity of hemiplegia with experimentally produced decerebrate rigidity, the localization of the lesion in the former case is not strictly comparable with that obtaining in the latter. It is not possible to enter into this question here, further than to refer the reader to a paper in which the present writer has reviewed the evidence in favour of the analogy between clinical and experimental states [18].

(1) *Conditions governing the occurrence of associated reactions.*—(*a*) In the reacting muscles of the hemiplegic side. In none of the

flaccid cases examined was any sign of an associated reaction in arm or leg detected. In the spastic cases, on the other hand, a more or less well-developed reaction on forceful voluntary activity of the normal limbs was constant. In two cases, indeed, no excursion of the paralysed arm occurred, but palpation revealed a distinct access of spasticity during the performance of the voluntary movement. We may say, therefore, that some degree of hypertonus in a case of hemiplegia is an essential preliminary to the development of an associated reaction. To this we may add that, in general, the higher the degree of spasticity present, the more forceful and the longer lasting will the associated reaction be. The force of the reaction cannot always be measured by the actual excursion of the limb. The most ample reactions of the kind were observed in a patient in whom spasticity was not very pronounced, but although of considerable amplitude they were not very forceful. The force of the reaction bears no relation to the degree of voluntary power retained by the affected limb, and in many instances far exceeds this and involves segments of the limb in which no voluntary activity remains—notably the forearm and hand.

(*b*) The nature of the voluntary activity necessary to invoke them. The form of voluntary muscular effort most effective in the production of associated reactions is forceful tonic contraction of muscles. No actual excursion of the parts acted upon by these muscles is essential. Thus a strong and maintained grasp of the normal hand is one of the most powerful stimuli for the reaction in the paralysed arm. Further, alternating movements, e.g., of the normal arm, when carried out rapidly and with a minimum of force do not commonly produce any associated reaction in the affected arm. However, a series of forceful punching movements of the normal arm does produce an associated response. Cutaneous stimuli, tactile or painful, have no effect, and the reflex movement that may result from such stimulation (Riddoch and Buzzard) bears no resemblance to the ordinary associated reaction now under discussion. In short, the adequate stimulus for an associated reaction in the muscles of the hemiplegic half of the body is strong tonic voluntary muscular contraction. Alternating movements are effective only when they are forceful and of a kind demanding widespread synergic fixation of the musculature. Even in these circumstances, the associated reaction is tonic and has no alternating character. Passive movements of the limbs have not been found effective in producing associated reactions.

We have chosen tonic voluntary activity of the normal limbs as the type of stimulus most effective in eliciting an associated reaction, but it is not suggested that voluntary contraction of other muscles may not have a similar, if less pronounced, effect. Firm clenching of the jaws, stiffening of the neck muscles, and such quasi-involuntary activities as yawning and stretching and coughing, also produce associated reactions. Further, voluntary contraction of one of the limbs on the hemiplegic side may be productive of an associated reaction in the other. It is possible also that the elevation of the shoulder, abduction of the arm and flexion of the forearm, which may accompany the attempt of the patient voluntarily to extend his clenched fingers in the affected hand, may be of the nature of an associated reaction. In this case, however, as we shall see when discussing Marie and Foix's classification of "syncinésies," another type of movement may be in question. In every instance the voluntary contraction which constitutes the stimulus for an associated reaction, whether it be in the limb or trunk muscles, must be forceful and maintained.

(2) *The form of the associated reaction.*—As Riddoch and Buzzard have pointed out, the associated reaction may be very widespread, but it is with the limb reaction that we shall mainly deal, because this is more readily capable of accurate observation and recording than a tonic contraction in trunk muscles, and is therefore better adapted for the determination of the nature of associated reactions as a whole. As we shall see later, it is essential in studying associated reactions that the conditions of examination shall be constant. The following brief description applies to the reactions obtained from a patient lying on his back with the head in the median position. The normal arm lies extended and supported on the bed at the patient's side. The hand is then held by the observer and the patient commanded to give a strong, steady, and maintained grasp. No excursion of the arm occurs. In these circumstances the paralysed arm as it lies resting, semiflexed, across the patient's body, is seen to go into strong tonic contraction after a short interval. In this contraction every muscle of the limb and limb girdle may be both felt and seen to contract. In the majority of instances the flexors of the forearm are most affected, a slow movement of flexion at the elbow results, and the new posture taken up is maintained more or less steadily until the patient is told to relax the voluntary grasp. In addition to flexion of the elbow there is frequently some elevation of the shoulder and either adduction or abduction of the upper arm. In the former case the forearm and hand pass across the body towards the sound side, in the latter the forearm is lifted from

the body and moved away from the normal side. Practically always the fingers and wrist go into more pronounced flexion than was initially present, and the forearm rotates slightly towards the supinated position. The reaction in the paralysed leg is one of tonic extension with inversion and dorsiflexion of the foot and dorsiflexion of the hallux. Less frequently seen is extension at the elbow with full pronation of the forearm and some flexion of the hip, less of the knee and the dorsiflexor response of the foot and hallux already mentioned. Again, in some cases, the upper limb reaction may consist in general tonic rigidity with a movement entirely of adduction or of abduction of the upper arm. It has been said by earlier workers that for a given patient the reaction is invariable, but my observations do not altogether confirm this, for from time to time, the conditions remaining constant, flexion may be replaced by extension in the upper limb. If, however, the conditions are changed, then the associated reaction may undergo even more striking variations, which we shall discuss in a subsequent chapter.

(3) *Effect of form of voluntary movement on associated reaction.*— In many patients the form of the associated reaction does not vary according to that of the voluntary movement or posture eliciting it, and a stereotyped reaction is obtained, whether the voluntary activity be a powerful grasp with the arm extended, or tonic contraction of the limb flexors or extensors against the resistance exerted by the observer However, this is not always nor even generally the case, and the subjects examined differed widely in this respect. In one case tonic flexion and extension of the whole normal arm against resistance, and tonic activity of each segment of the limb separately and in both directions was tried, but in every test, whether the normal fingers were being extended against resistance or the elbow flexed, the same response was seen in the paralysed arm, namely, increased flexion at the elbow, abduction and elevation of the upper arm, slight supination of the forearm and increased flexion of wrist and digits. In other subjects, however, the form of the associated reaction could be completely modified according to the form of the voluntary movement of the sound arm. Thus voluntary flexion of the elbow against resistance evoked associated crossed flexion, while voluntary extension evoked ample associated extension (fig. 1).

Rarely, a given case may show a crossed associated reaction of opposite direction to the voluntary movement evoking it. Thus voluntary flexion is followed by associated extension and voluntary extension by flexion. This is true also of voluntary adduction and abduction of the upper arm, although in this case a symmetrical response is no more commonly seen than one of opposite sense.

In one patient, the influence of reversing the form of the voluntary movement was less potent in modifying the associated reaction. Thus, voluntary flexion of the normal arm produced associated flexion, while voluntary extension produced a rapid oscillation of the flexed forearm in the initial posture (fig. 2).

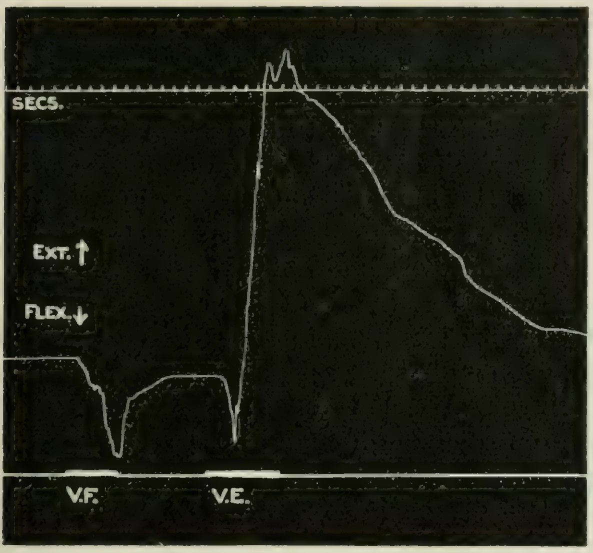


FIG. 1.

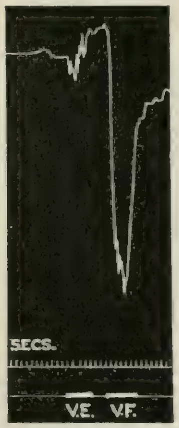


FIG. 2.

FIG. 1.—Inversion of form of associated reaction in hemiplegic arm on reversing form of voluntary movement. The voluntary activities were flexion of the normal against strong resistance followed by extension against resistance. Voluntary flexion (V.F. on signal record) is followed by associated flexion, and voluntary extension (V.E.) by associated extension. In the particular subject from whom this record was taken, the associated extension was commonly preceded by a transient flexion. All the records reproduced here were made with a vertically moving lever, the writing point of which was arranged vertically above that of the signal lever, and with the exception of fig. 4 they are one-third the amplitude of the actual excursion of the limb. Upward movement indicates extension and downward movement flexion (cf., Appendix). All the records are reduced to two-thirds their original size.

FIG. 2.—Modification in form of associated reaction on reversal of form of voluntary movement. The voluntary activities are as in the case of fig. 1, but extension precedes flexion. Voluntary extension (V.E.) produced a clonus-like oscillation and increased spasticity of the arm without any excursion of the forearm, while voluntary flexion (V.F.) evoked associated flexion.

In the case of the lower limb, the tendency to a stereotyped reaction was found to be more marked than in that of the upper limb. In the majority of cases the associated reaction was that already described, namely, limb extension, but in several patients flexion at hip, knee and ankle (dorsiflexion) was constant irrespective of the form of the voluntary movement. Even here, however, a reversal of form of the associated reaction was occasionally observed in response to reversal in the voluntary muscular effort eliciting it. When voluntary flexion or extension was in question, the associated reaction was in some cases symmetrical, and in others opposite in form. In the case of abduction and adduction, however, as Raimiste [7] long since pointed out, the associated reaction is generally symmetrical, voluntary adduction being accompanied by associated adduction and conversely. Even this reaction was poorly developed at times, and it has to be remembered that in most cases of residual hemiplegia there is considerable voluntary power in the affected leg, and that it is impossible in these circumstances, and even in the normal subject, to adduct or abduct the extended limb without also bringing into action with equal force the corresponding muscles of the crossed leg.

The lower limb when under observation for associated reactions has to be supported by the observer in such a manner as neither to impede nor to facilitate unduly any reaction which may develop. When graphic recording is in question the limb has to be slung from the ceiling. It is obvious that by reason of its mass and length the lower limb is not well adapted to careful investigation, and possibly a more perfect technique might reveal that the tendency to constancy of reaction is less complete than at present seems to be the case.

In one patient reversal in the form of a tonic voluntary effort in the paralysed leg inverted the form of associated reaction in the paralysed arm, voluntary flexion against resistance leading to associated flexion and vice versa (fig. 3).

In this connection it is interesting to note the form of associated reaction in the paralysed arm which accompanies yawning and stretching. It is exceptional to find a subject with residual spastic hemiplegia from whom a history of spontaneous movement of the paralysed arm or hand on yawning cannot be obtained. In many cases, coughing is also accompanied by such a reaction. Every patient whom the writer has questioned on this point, with a single exception, has stated that the movement of the hand and digits in these circumstances is one of extension. This is often complete and is accompanied by fanning of the fingers. The forearm may be extended, but more commonly flexes and is raised up in front of the patient. Whenever the writer has observed this reaction to yawning, extension and separation of the digits have occurred. Moreover, two patients volunteered the statement that when the fingers are extended and abducted during a yawn, they are able to flex and extend them rapidly, a thing they were unable to do at any other time. Indeed, one man added that he always waited for a yawn so that he might exercise his fingers in this way. In an earlier reference to this detail [17], the general inference was suggested that unilateral muscular contraction evoked an associated flexion, while such bilateral muscular acts as yawning evoked associated extension. In the light of the more recent observations recorded here, this generalization must be abandoned, yet it remains a striking fact that the form of muscular activity most commonly producing associated extension of the digits is bilateral. In this case, the stimulus may be tonic contraction of the diaphragm.

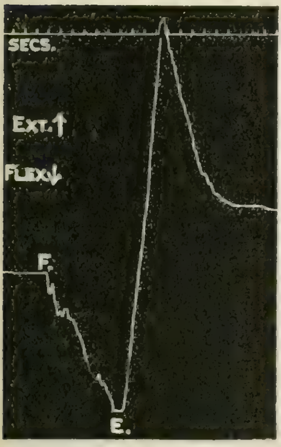


FIG. 3.

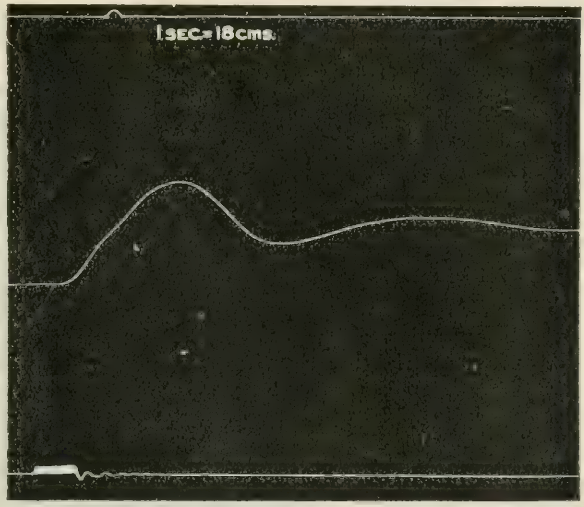


FIG. 4.

FIG. 3.—Inversion of associated reaction in hemiplegic arm on reversal of form of voluntary movement of homolateral leg. At F, voluntary leg flexion evoked associated flexion in the arm. At E, the leg is powerfully extended against resistance and associated extension in the arm occurs.

FIG. 4.—Graphic record of supinator jerk from hemiplegic arm of patient from whom figs. 1, 3, 6 and 7 were also taken. With the method of determining latency which was adopted (cf. Appendix) the latent period is seen to be 0·04 second (40 σ). With the same method, the latency of associated reactions and other tonic reflexes described is seen to be much longer. With a more perfect technique, Jolly found the average latency for the knee-jerk in man to be 0·02 second.

(4) *The latency and duration of the associated reaction.*—When we come to consider the latency and duration of associated reactions we gain an insight into their probable nature. In a large series of obser-

vations, the following values were obtained for the latencies in different cases: 0·25, 0·5, 0·75, 1·0, 1·5, 1·75, 2·0 seconds. If we compare this with the latency of such a phasic reflex as a tendon jerk, the contrast is striking. Fig. 1 is the graphic record of two associated reactions (flexion and extension at the elbow) in the hemiplegic arm of a patient whose supinator jerk is recorded in fig. 4. The method of obtaining the latency was the same in the two instances. The latent period of the associated movement is 0·75 second, while that of the supinator jerk is 0·04 second. It will be noticed that both records show the characteristic " shortening reaction " of tonic muscle.

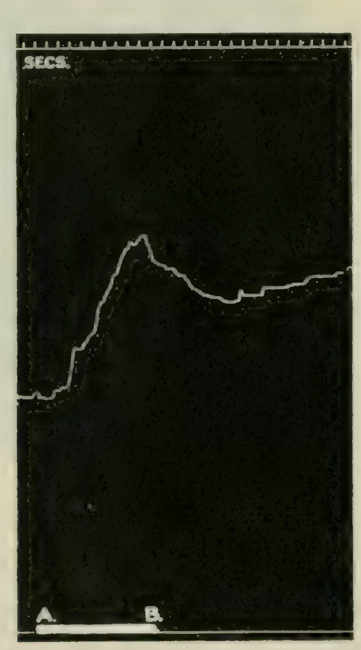


FIG. 5.—Associated reaction in hemiplegic arm from a patient with infantile hemiplegia. The tonic after-contraction persisted for over 40 seconds. The first 18 seconds are seen in the record. The stimulus—a forceful grasp of the normal hand—is seen to have lasted 10 seconds (A—B).

The duration of an associated reaction is roughly that of the voluntary movement or contraction evoking it, but there is in some instances a prolonged after-contraction or tonic prolongation of the spasm which may last for several seconds. In one case this was still of undiminished intensity after the lapse of 40 seconds (fig. 5).

While the reaction persists, the limb maintains the new attitude more or less steadily, but occasionally there may be a fine tremulous oscillation round a fixed point. In one instance the rate of this oscillation was 6 per second, and the tremor resembled the ordinary clonus of a spastic limb.

In general, it may be stated that the more spastic the limb, the longer the latency and after-contraction, though the amplitude of the limb excursion may be small. In one case in which spasticity was slight, the latency was always less than a second, commonly 0·25 second, the limb excursion was ample and rapid in rise and there was practically no after-contraction, the limb having returned to its initial position within 0·5 second of cessation of the stimulus (grasp of normal hand).

(5) *Inferences as to the nature of the associated reactions.*—We have seen that associated reactions are evoked most typically by voluntary tonic contraction of muscles. They are not produced by rapidly alternating voluntary movements unless these are widespread or forceful, and they cannot be produced by cutaneous stimuli apart from such tonic contraction. In short, the adequate stimulus is proprioceptive and of some duration. The response has a comparatively long latent period, is commonly slow in development and lasts, and may outlast, the duration of the stimulus. The reacting muscles go into strong tonic contraction, which produces, with rare exceptions, an excursion of the limb of variable amplitude. The limb takes up a new posture which persists until the stimulus producing it ceases. Therefore, in respect of stimulus, latency, form and duration the associated reaction presents all the characters of a tonic or postural reflex. Usually, the seat of the stimulus is the musculature of one of the normal limbs, but strong voluntary contraction of a partly paralysed leg may give rise to a well-marked associated reaction in the homonymous arm.

Chapter III.—Other Tonic or Postural Reactions in Hemiplegia.

We have learned from the researches of Sherrington and Magnus that decerebrate rigidity and normal tone may be influenced by afferent impulses arising in the labyrinths and in proprioceptive end-organs in the musculature and other deep structures of the neck and body wall. The function of these reflex variations in muscle tone is to produce the various attitudes of the animal. If, therefore, the spasticity of hemiplegia is physiologically identical with decerebrate rigidity, we should expect to find evidence of these reactions in the affected muscles in cases of hemiplegia. Indeed, several observers have recorded such reactions in man (Magnus and de Kleijn [3] [4], Brouwer, Marie and Foix [6]). While we may safely conclude that the occurrence of tonic neck reflexes in man has been established in various clinical conditions, labyrinthine reflexes have been much less frequently observed, and in the majority of cases in which neck reflexes have been recorded there have been no clear indications of labyrinthine influence on tone.

(1) *Tonic neck reflexes.*—In the spastic cases examined for these reactions, the general rule was that at the beginning of the investigation, and with the patient standing, rotation of the head on the neck produced no excursion of the hemiplegic arm, and it was not until the examination of the associated reactions had been carried out, the patient placed in a supine position, or vigorous passive movements of the paralysed arm performed, that active neck reflexes developed. Occasionally, however, these reactions were very facile and active from the outset. As the patient stood erect with the affected arm semi-flexed and adducted, voluntary rotation of the head to the paralysed side, especially if carried out with force, evoked a slow but powerful tonic extension of the arm, which was maintained until the head was turned back again to the median position, or across to the normal side. Associated with the extension, the arm was generally slightly advanced and adducted, and the forearm went into full pronation. The wrist extended and the fingers clenched tightly. Rotation of the head from the paralysed side, or from the median position, so that the patient looked over the normal shoulder, was followed by a movement of flexion of the forearm and slight return to supination. The upper arm was commonly adducted, but in some patients there was abduction and elevation. The form of this tonic reaction, both to direct observation and in a graphic record, was very characteristic. The latent period was distinctly long, and the following values were obtained in different patients under the same conditions of recording: 1·0, 1·25, 1·6, 2·0, 3·5, 5·0, 6·0 seconds. From the moment of onset of the response to that of maximal excursion of the reacting limb, a period of from 0·5 to 2 seconds elapsed, but in this respect there was considerable individual variation. In one patient, after a latent period of about 1 second the limb shot rapidly into its new posture, remained there for from 5 to 6 seconds and then returned to its initial attitude. In general, however, the new posture was maintained until the patient turned the head back to the original position (fig. 6).

Care was taken to ensure that in rotating the head the subject did so steadily and without jerking, and the average period during which the movement of rotation was carried out was from six to ten seconds. It was when the movement was well under way that the slow movement of the reacting arm to its new posture began.

In two patients passive rotation of the head by the observer evoked forceful variations in the attitude of the paralysed arm and leg, but, in general, voluntary movement was essential.

At some period of a systematic examination of the postural reactions, or in some at least of a series of such examinations, these tonic neck reflexes were present in greater or less degree in every patient examined. When they were not evident at first, the practice was to make the patient lie on his back on a couch for a few minutes, after the lapse of which the reactions began to appear on appropriate stimulation, that is, on rotation of the head. There could be no doubt that their appearance was facilitated by a preliminary examination of the associated movements, and it was found that after half an hour's examination and manipulation of the paralysed arm the reactions were at their maximum for the individual patient. When fully developed,

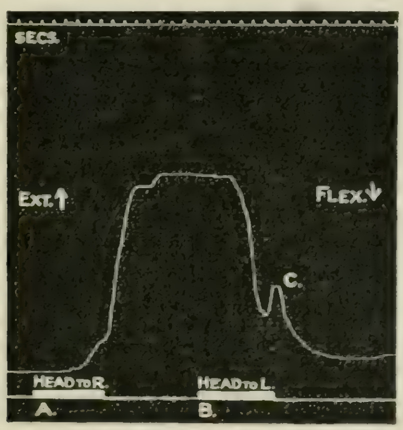


FIG. 6.—Tonic neck reflex in hemiplegic arm. At A on signal line, the head was voluntarily rotated to the paralysed side through an angle of approximately 180 degrees from its initial position with the face looking over the normal shoulder. After a latent period of about two seconds, and while rotation was still in progress, a tonic extension developed in the arm. At B, the head is rotated back to its initial position, and again after a similar latent period the tonic extension gives place to tonic flexion, the arm regaining its original posture of semi-flexion at the elbow. During this return a short spasm of extension is seen to occur at C. The head rotation occupied six seconds and was carried out without undue force.

rotation of the face towards the paralysed side evoked extension, and rotation to the sound side flexion. This result is in strict accord with Magnus's observations.

Inclination of the head to one side ("Wendung" in Magnus's nomenclature) was not found to evoke any reaction in the cases so far examined, but it is possible that further investigation may reveal a neck reflex evoked in this way. In the case of the lower limb, the influence of variations in head posture in relation to the trunk was distinctly less constant, and when present less marked than was the case with the upper limb. The commonest finding is that rotation of the head produces an increase in extensor rigidity in the paralysed leg, whether rotation be towards or away from the paralysed side. In one patient, however, with a profound degree of right hemiplegia from cerebral tumour, active and passive rotation of the head towards the paralysed side evoked powerful extensor spasm in both arm and leg, and rotation to the normal side evoked active flexion spasm in the arm, and a pronounced diminution of extensor spasm in the leg.

Finally, when head rotation seems to be entirely without effect, the presence of a latent influence on limb tonus can be demonstrated for the paralysed limbs by eliciting associated movements with the head in different positions. Observations in this sense have been reported by Simons [12] [13], and the writer's own results are in strict accord with those recorded by him. This effect will be described in the following chapter.

(2) *Tonic labyrinthine reflexes.*—In the decerebrate animal, the reinforcing influence of the labyrinths on extensor tonus in the limbs was found by Magnus and de Kleijn [3] to be minimal when the animal is in the standing position and the head so held that the line of the mouth ("Mundspalte") makes an angle of about 45 degrees below the horizontal, and maximal with the animal in the supine position and the line of the mouth making an angle of about 45 degrees above the horizontal. In an infant with amaurotic family idiocy examined by these observers, both neck and labyrinthine reflexes were found to be very active, and they were able to determine that the maximal and minimal positions were practically identical for the human subject with those found for quadrupeds (cat, dog, monkey). In hemiplegia, therefore, we should expect to find labyrinthine influence maximal with the patient in the supine position and the head slightly retracted, and minimal with the patient standing, sitting or prone, when the face points downwards to the ground and a perpendicular drawn out from the face making an

angle of about 45 degrees below the horizontal. This, in fact, is what has been found to be the case, as observations recorded in a later chapter indicate.

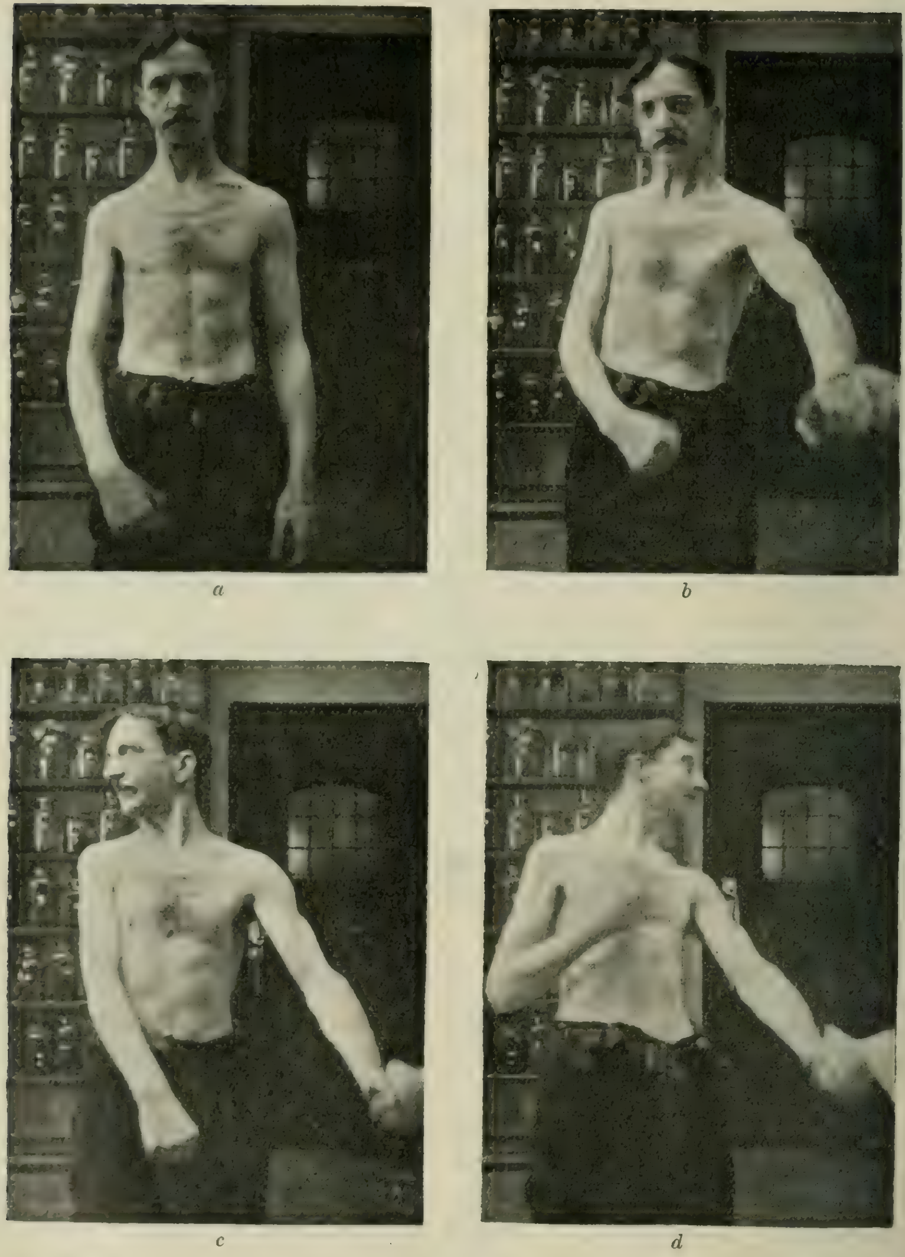
In the cases under examination, fully developed labyrinthine reflexes were not observed. The clearest indications were obtained from two patients with right hemiplegia (one thrombotic in origin, and one the result of compression from cerebral tumour). In the former, laying the subject on to his back from a sitting position evoked no active extensor tonus in the affected arm, but when he lay prone and the arm hung over the side of the couch, it was clear that it had taken up a posture of increased flexion at the elbow, despite the action of gravity, now that labyrinthine influence on extensor tone was minimal. In the latter, laying her back into the supine position from a sitting position evoked a marked and forceful extension spasm in the previously flexed arm. It was not possible to examine her in the prone position, as the ordinary hospital bed is not suitable for the purpose and she could not well be moved on to the hard narrow couch used for this purpose.

We have seen, however, that even in those patients where tonic neck reflexes cannot be demonstrated directly by simple head rotation, the existence of strong tonic influences arising in the neck proprioceptors can be demonstrated by studying the profound modifying effect on associated reactions of head rotation. This is equally true of labyrinthine influence, and the investigation of associated reactions with the patient in the lateral, prone and supine positions indicates that the labyrinths do influence tone in the hemiplegic arm, if not very obviously in the leg. The results of these tests will be described when we are considering the interaction of the various tonic reflexes.

CHAPTER IV.—INTERACTION OF TONIC REFLEXES.

We have said that in those cases where rotation of the head on the neck and variations in head posture in relation to the horizontal plane do not evoke tonic reactions in the hemiplegic limbs, that nevertheless both neck and labyrinthine influences are at work and can be demonstrated by studying the effect of changes in head posture in relation to trunk and to space on associated reactions obtained in the manner described. We shall now proceed to study some examples of this interaction of tonic reflexes.

(1) *The influence of neck reflexes on associated reactions.*—When the neck reflexes are active, the familiar associated flexion of the hemiplegic



a *b* *c* *d*

FIG. 7, *a*, *b*, *c*, *d*.—Inversion of associated reaction in hemiplegic (right) arm by neck reflexes: *a* = resting position of hemiplegic right arm; *b* = flexion-adduction reaction to a forceful grasp with the right hand with the head in the median position; *c* = extension-adduction reaction with full pronation of the forearm, when the head is rotated towards the hemiplegic side; *d* = flexion reaction when the head is rotated to the normal side.

arm on forceful tonic contraction (grasp) of the normal arm may be completely inverted in form when the head is rotated to the hemiplegic side, that is, with face pointing over the shoulder of the affected half of the body. The photographs below (fig. 7 (*a*), (*b*), (*c*), (*d*)) show this more clearly than any verbal description. This patient has a cerebral thrombosis of five years' standing. An identical state of affairs is revealed in fig. 8. This graphic record is taken from a case of embolic left hemiplegia of two years' standing. It shows in addition to reversal in form of associated reaction, the "shortening reaction" so characteristic of reflexes in tonic muscle. After cessation of the voluntary grasp of the normal hand, the associated flexion or extension passes off incompletely, but with rotation of the head the limb returns at once to

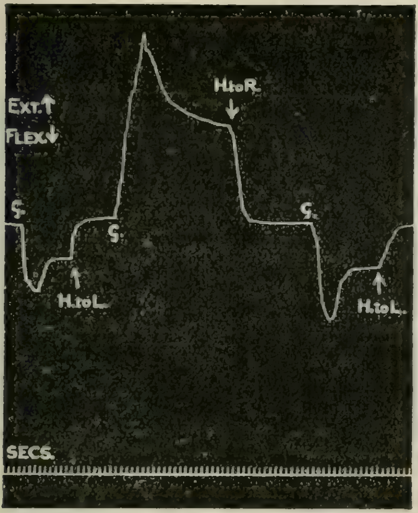


FIG. 8.

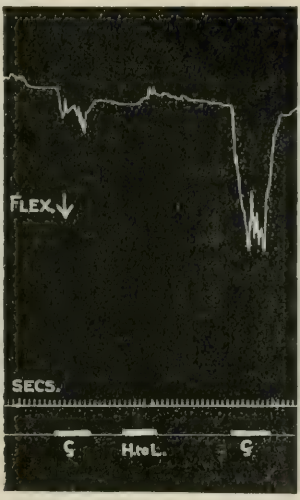


FIG. 9.

FIG. 8.—A graphic record of the same phenomena from a patient with left hemiplegia. The initial posture of the head is full rotation to the right (normal side). At G a voluntary grasp with the normal hand evokes associated flexion of the hemiplegic arm with incomplete return ("shortening reaction") on relaxation of grasp. The head is then rotated to the hemiplegic side (H to L). At once further extension to the original posture of the arm occurs. At G, a grasp with the normal hand is now accompanied by strong associated extension in the hemiplegic arm with incomplete return on cessation of grasp. The head is again rotated to the normal side (H to R), and the arm returns to its original posture. At G, voluntary grasp with the normal hand is followed by associated extension and incomplete return as at the beginning of the record. Therefore, the record shows inversion of associated reaction by neck reflex, and also the characteristic "shortening reaction" of tonic muscle.

FIG. 9.—Shows a less profound influence of neck reflex on form of associated reaction than is seen in fig 8. A case of right hemiplegia. With the head rotated to the hemiplegic (right) side, voluntary grasp evokes a clonus-like oscillation of the hemiplegic arm in its initial posture. On rotation of head to normal (left side), the associated reaction is flexion.

its initial posture. However, the influence of the neck reflexes is not always so potent, and in some subjects the associated reaction is modified but not inverted. Thus, fig. 9, taken from a patient with right hemiplegia of thrombotic origin, shows an associated reaction consisting simply of increase of tone and oscillation of the limb round the initial posture when the head is rotated to the paralysed side, but associated flexion when the head is rotated to the normal side. With the head in the median position a slighter degree of flexion occurred. Fig. 10 records an even less marked influence of the neck reflex. The patient had a thrombotic right hemiplegia of two years' standing. In both positions of the head (rotation to right and to left) the associated reaction in the affected arm was flexion, but with the head rotated to the normal side the flexion was more ample and more forceful than with the head rotated to the paralysed side. In the latter instance, each successive associated reaction is less ample and the return to the initial posture less complete, so that the angle between forearm and upper arm gradually opens out. Finally (grasp 9), the head is again rotated to the

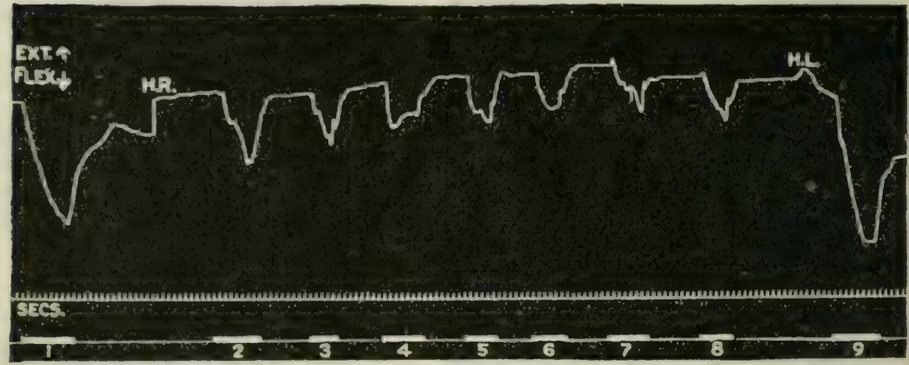


FIG. 10.—Shows a still less marked influence of neck reflex on the associated reaction of the hemiplegic arm. The reaction is not inverted in form, but the associated flexion is diminished progressively in amplitude and force with each successive grasp after the head has been rotated from the normal to the hemiplegic side. Rotation of the head to the normal side after a series of voluntary grasps produces on a further voluntary grasp a full flexion reaction in the hemiplegic arm. The first and last (1 and 9) associated flexion reactions were obtained in the manner described with the head rotated to the normal side. The head was then rotated towards the paralysed side, and a series of grasps performed with the normal hand (2 to 8). A progressive diminution of the associated flexion is seen with each grasp, and the base line rises, indicating a gradual opening out of the angle between forearm and upper arm. On rotating the head back again towards the normal side, a greatly increased flexion reaction at once ensues on grasping. This reaction is more ample than the original one, and may be said to show the phenomenon of "post-inhibitory exaltation." Further, a "shortening reaction" is to be seen after the first and last reaction.

normal side and a more ample associated flexion than was present originally is seen to occur. This increased amplitude may be regarded as an example of "post-inhibitory exaltation."

(2) *The influence of labyrinthine reflexes on associated reactions.*—This is best seen by examining the associated reaction in the hemiplegic arm with the patient in the positions of maximal labyrinthine influence (supine) and of minimal labyrinthine influence (prone). In the patient whose reactions are illustrated in fig. 7, the associated reaction with the patient standing and the head in the median position is slight flexion at the elbow. In the supine position, on two separate occasions, the reaction was extension, pronation and slight advancement of the upper arm. On these two occasions, on turning the patient over on to his face (prone), with the head slightly retracted and the arms hanging free at the sides of the narrow couch, the hemiplegic arm at once took up a posture of increased flexion, despite the unantagonized action of gravity on the limb. In these circumstances, the associated reaction was ample flexion with some abduction at the shoulder. Similar results were obtained with the patient sitting upright in a chair. When the head was well thrown back (maximal position of labyrinthine influence) and in the median position, the associated reaction was extension of the affected arm, but with the patient sitting well forward and the head bent downwards and the face gazing between his knees (minimal labyrinthine influence) the reaction was flexion.

Apart from this direct modifying effect of labyrinthine impulses on the form of the associated reaction, a general reinforcing effect upon both neck reflexes and associated reactions often follows placing the patient in the prone position, and this also we may attribute to the labyrinthine influence on tone.

(3) *The interaction of associated reaction, neck and labyrinthine reflexes.*—It is clear from what has been said that at any given moment an associated reaction is the resultant of at least three factors: the form of the stimulus (voluntary tonic contraction), the position of the head in relation to the horizontal plane (labyrinthine influence) and the position of the head in relation to the trunk (neck influence). It follows, therefore, that in an examination of associated reactions in which none of these factors is constant we may obtain a bewildering diversity of reactions in the hemiplegic arm, which seem to be governed by no very evident laws. In the study of associated reactions undertaken in 1912-1914 only one of these factors, and that not the most important, was taken into account. It was observed that sometimes

a reversal in the form of the voluntary effort eliciting the associated reaction did effect a reversal in the form of the latter, but this was not constant, and sometimes the reaction was symmetrical and sometimes in the opposite sense. We can see now, however, that no constancy of result was to be expected unless and until the influence of head posture was taken into account. In one of the patients of the first series a stereotyped associated flexion of the hemiplegic arm was obtained no matter what the form or the situation of the voluntary effort evoking it. The observation now gains interest, for the record contains a note that the patient always turned his head to the right (normal side) when carrying out any forceful voluntary movement. It is not too far-fetched, perhaps, to conclude that this rotation of the head away from the paralysed side was a determining factor in the constant form of the associated reaction.

Since labyrinthine and neck influence are always in question, it follows that in the different positions of the subject they must combine variously, sometimes reinforcing and sometimes antagonizing each other. This can be tested by examining associated reactions with the patient in the supine, prone and lateral positions with the head in the median, right and left relations to the trunk. This somewhat complex examination is best illustrated by an actual example. A. C., a case of thrombotic right hemiplegia (cf. figs. 1, 3, 6, 7).

First position—standing. Arm hangs as in 7, *a.* Voluntary movement throughout examination consists in a forceful voluntary grasp with the left hand, the left arm being extended and adducted and slightly advanced.

Head centre = slight flexion at elbow.
Head right = extension, pronation and advancement.
Head left = flexion at elbow.

Second position—supine. Arm slung in same degree of flexion as fig. 7, *a.* Voluntary movement as in 1. Head slightly retracted.

Head centre = some extension, pronation and adduction.
Head right = full extension and pronation.
Head left = flexion to right angle.

Third position—prone. Arm hanging free at side of couch and flexed to an angle of about 120 degrees with upper arm. Head slightly retracted. Voluntary movement as above.

Head centre = flexion to right angle with slight abduction.
Head right = moderate extension with marked adduction.
Head left = full extension with pronation and slight adduction.

Fourth position—right lateral. Elbow lies on couch anterior to trunk in moderate flexion. Voluntary movement as above.

Head centre = flexion.

Head right (i.e., face looking downwards on to pillow, occiput above) extension.

Head left (face up, occiput down) extension.

Fifth position—left lateral. Hemiplegic arm now uppermost and slung in moderate flexion. Voluntary movement as above.

Head centre = flexion.

Head right (i.e., face up, occiput down) = extension.

Head left (i.e., face down, occiput up) = flexion.

These results become intelligible if we bear in mind that labyrinthine influence on extensor tone is maximal with the head slightly retracted and the face looking upwards, and minimal with the head slightly retracted and the face looking downwards. Therefore, with the patient supine we should expect to find an extensor reaction (if labyrinthine reflexes are active) with head centre as well as with head right (i.e., turned to paralysed side). In the prone position, on the other hand, labyrinthine influence being minimal, we should expect to find neck reflexes predominating and a flexor associated reaction with head centre and head left. This is what we have actually found to be the case. In the lateral positions with the head median, labyrinthine influence is intermediate in potency (less than in supine and more than in prone positions), and here the neck reflexes determine the form of the associated reaction. With the face pointing upwards, however, labyrinthine influence increases and we see associated extension in both lateral positions, though in the right lateral position this involves rotation away from the paralysed side. With the face pointing downwards labyrinthine influence is minimal, and here again the neck reflexes determine the form of the associated reaction. Therefore, in the right lateral position we get associated extension when the face points downwards (that is, head rotation to right) (paralysed) side, and in the left lateral position with the face pointing downwards (head to left) (normal) side we get associated flexion.

We see, therefore, that a rapid method for determining the relative predominance of labyrinthine and neck reflexes in a case of hemiplegia, is to place the patient in that lateral position in which the hemiplegic side is downmost and the normal side uppermost. If, in these circumstances, rotation of the head so that the face points upwards produces associated extension in the hemiplegic arm (that is, when face is turned away from hemiplegic side) then the labyrinthine influence is present and active. If, however, flexion results then the neck reflex predominates.

One further complicating factor remains for mention. If each of a series of patients is subjected to repeated examination on different days, it may be found that on one occasion the neck reflexes predominate in all positions of the head in space, while on another the labyrinthine influence is the more potent. As was observed before [15] when dealing with the reflex phenomena in spastic paralysis of the lower limbs, reflex reactions in tonic extensor muscles vary far more widely from day to day than the phasic reflex reactions obtained from flexor muscles.

Thus in a spastic paraplegia in extension, the form, receptive field and activity of the flexion reflex varies little if at all from day to day, but the degree of spasticity, the presence of clonus and of other reactions in the extensors is much more variable. This is equally true of the tonic reflex reactions now under consideration. The conclusion to be drawn from this is that repeated examination on different occasions is essential if we are to obtain a clear notion of what tonic reflexes are present in a given subject with hemiplegia. Such variations as may be detected from day to day, however, do not indicate that associated reactions are capricious phenomena governed by no discoverable laws. They indicate that there are several factors at work in determining the form of an associated reaction, or the presence and activity of a tonic neck or labyrinthine reflex; that the relative potency of these different factors varies slightly from day to day and from hour to hour, according to the external circumstances (such as external temperature, fatigue, &c.) obtaining; and that patient and repeated examination will reveal that four determining factors are always operative, though in varying degrees of intensity. These factors are: (1) the form of the voluntary effort eliciting an associated reaction. This is relatively unimportant in our experience. (2) The presence of tonic impulses arising in the proprioceptors of the neck; (3) the presence of tonic impulses arising in the otolith organs of the labyrinths; and (4) the manner in which neck and labyrinthine influences combine.

Chapter V.—Relation of Associated Reactions to other Tonic Reflexes.

In our endeavour to determine the nature and physiological significance of associated reactions, we may compare them with the tonic neck reflexes, for it is undisputed that these are reflex postural reactions. From the observations recorded here there can be little doubt that the familiar associated reactions of the paralysed limbs in hemiplegia are phenomena of the same order as the tonic neck reflexes of Magnus and de Kleijn. An observer looking at an associated reaction in the paralysed arm produced by a tonic grasp with the normal arm, and comparing it with the tonic neck reflex occurring in the paralysed arm on rotation of the head, cannot distinguish the two; they are identical in form, latency and duration. If there be any distinction between the two, as they occur in a given subject, it is that the tonic neck reflex tends to have a slightly longer latency, to develop more slowly, to have a longer after-contraction and to subside less suddenly. These points of difference, which are never more than a matter of one or two seconds, can readily be traced to the character of the stimulus in each case. In the associated reaction, the stimulating grasp is more forcible, develops more rapidly and ceases more suddenly than is the case with the leisurely rotation of the head which produces the tonic neck reaction. In both instances, the limb goes into strong tonic contraction, predominantly flexor or predominantly extensor as the case may be, and takes up a new posture which is maintained until the proprioceptive stimulus ceases. We may conclude, therefore, that the associated reactions which follow strong tonic voluntary muscular contraction in hemiplegia are postural reflexes closely allied with the tonic neck and labyrinthine reflexes of Magnus and de Kleijn.

In the introductory chapter we mentioned the pioneer observations of Sherrington that the tone of a given muscle, although dependent for its maintenance on the afferent nerve supply of that muscle, yet was capable of modification, or regulation, by means of afferent impulses arising elsewhere. As we have seen, the later work of Magnus and his collaborators has resulted in the minute analysis of the nervous reflex mechanisms by which this regulation of tone is carried out. However, these observers make no reference to tonic reflexes arising in the limbs themselves and regulating the posture either of the head, trunk or limbs. Yet a moment's consideration will suggest that the existence of such reactions is extremely probable, for voluntary activity of the limbs may be such as to demand widespread synergic postural fixation, and it is the experience of everyone that such fixation occurs in all forcible muscular activities of the limbs. Moreover, we do not turn in vain to experimental physiology for confirmation of these conjectures. Sherrington [9] has recorded that "The reflex posture in each body-region is not of course wholly independent of afferents in other regions. Thus, passive flexion of the elbow and shoulder often provokes in the decerebrate preparation heightening of the tonic extension of ipsilateral knee and ankle, and lowering of it in crossed knee and ankle. Again, active or passive rotation of neck on its long axis in the decerebrate preparation inhibits extensor tonus in hind-limb on the side of the lowered pinna and causes active flexion of the knee . . . ." Here we find grouped together, as reactions of the same order, tonic reflexes arising in the limbs and acting on the limbs, and tonic reflexes arising in the neck and acting on the limbs. This is exactly what we have described as occurring in hemiplegia. The associated reaction in the paralysed arm on voluntary clenching of the normal hand is a tonic reflex arising in the limb and acting on the (crossed) limb. When they are the result of contraction of trunk muscles, as in yawning, they may be called " tonic reflexes arising in the trunk and acting on the limbs." In the same way, the associated tonic reactions of the trunk muscles may be classified according to whether they depend upon voluntary contraction of trunk or of limb muscles.

If we accept this view as to the nature of " associated movements " in hemiplegia, we are not postulating as essential to the co-ordination of posture in man any factor or process which has not already been demonstrated to obtain in mammals, from the guinea-pig to the ape.

It is not necessary to recapitulate the reasons given in a previous chapter for regarding " associated movements " as tonic reflexes, but we may now emphasize, as further confirmation of that conclusion, the manner in which they act harmoniously with the tonic neck and labyrinthine reflexes, each group reinforcing and modifying the other two. Nevertheless, certain alternative interpretations have to be considered. Marie and Foix [6] speak of the reactions in question as " syncinésies globales," and regard them as one of three distinct types of associated movement to be observed in cases of hemiplegia. We are not now concerned with the second and third types, though it will be necessary to refer to them later. Marie and Foix state that " syncinésies globales " consist, as the term indicates, of a generalized contraction of the muscles of the reacting limb in which there is a struggle between flexor and extensor groups, one or other predominating and determining the direction of the movement. In effect, the result is simply an exaggeration of the type of spasticity already present in the limb, flexion in the arm and extension in the limb. They state further that for a given patient the form of the global associated movement is constant under all conditions and incapable of variation. Now, if we accept this view we seem compelled to deny that associated movements are reflex reactions, for in no known reflex is this complete overthrow of co-ordinated activity to be observed. All postural and phasic reflexes show either simple reciprocal innervation or the more complex double reciprocal innervation. In view of the observations here recorded, it seems impossible to deny the reflex origin of associated movements, and therefore we need not give further consideration to Marie and Foix's implication. However, it is the fact that antagonistic muscle groups, extensor and flexor, are to be observed in simultaneous contraction in such an associated reaction as we have described. Riddoch and Buzzard [8] have emphasized this point, and evidently felt the difficulty of reconciling it with their conceptions of reflex co-ordination of movement. Hence they came to the conclusion that while reciprocal innervation obtains in phasic reflexes, that is in reflex movements, postural reflexes are governed by a distinct process of concurrent innervation. It is not necessary to modify or add to the laws governing the reflex co-ordination of movement which have already been formulated. Sherrington [10] has pointed out that simple reciprocal innervation is "a relatively artificial reaction" because: "The isolated stimulation of just one whole afferent nerve, the rest of the nervous system lying plunged at the time in approximately complete quietude, is a state of things little resembling the ordinary occurrences of waking life. Usually in the latter the reactions of the nervous system result from the combination of a number of stimuli playing concurrently on its afferent channels, and some impelling to one action and some to another. Any particular motor centre, whether for flexion or extension, lies then under at least a twofold influence. . . . If we voluntarily hold the arm semi-flexed, nothing is easier than to make both flexor and extensor contract together; by simply feeling the hardness of the muscles through the skin we can assure ourselves of that fact. . . . Certain reflex reactions in their natural occurrence similarly exhibit in some cases a contemporaneous contraction of antagonists." If, in an experimental preparation, two stimuli, one exciting flexion and one extension of a limb, are simultaneously given, it is possible by suitable grading of the two to produce a flexion movement in which both flexors and extensors are simultaneously in contraction. What is observed is that flexion is less pronounced than it would have been with a single flexion stimulus, while inhibition of the extensors is also less complete. The discharge from both flexor and extensor half-centres represents the algebraical sum of the opposed excitation and inhibition. We see, therefore, that it is not right to assume "that under reciprocal innervation two antagonists necessarily can never be in contraction at the same time. . . . What reciprocal innervation does provide is that, in the execution of a muscular act by antagonists, augmentation of contraction or motor discharge shall not occur concurrently in protagonists and antagonists, nor conversely decrease of contraction or discharge occur concurrently in the two. These latter appear only possible when, breaking in on a condition of rest of both half centres or opponent muscles, there ensues one of those instances of double reciprocal innervation in which the balance between inhibition and excitation is such as to allow both half-centres to discharge, although unequally ; or when to such a state of double reciprocal innervation there succeeds a reversion of both half-centres into rest, the stimuli which evoked the double reciprocal innervation subsiding together. Except under these circumstances, reciprocal innervation secures that any increase in the contraction or discharge of the protagonists shall be accompanied by corresponding diminution of the contraction or discharge of its antagonist, even to complete suppression of the latter." It is scarcely possible to explain this complex process of reflex coordination of movement and of posture more succinctly, hence these long quotations from Sherrington may be pardoned. The relation of opposing groups of muscles in so complex a reaction may be summed up in the striking phrase of Hughlings Jackson, employed originally it is true in another connection, but equally apt in this, that there is between the two "a perfect co-operation of antagonism." We are not, therefore, compelled to reject as a true reflex reaction one in which there is visible simultaneous contraction in opposing muscle groups. Moreover, it is clear that in a maintained attitude this simultaneous activity will be more readily visible than in a rapid movement of the limb. In short, the final difficulty in regarding "associated movements" as true reflex reactions has been removed.

There remains one other possible interpretation. Socin and Storm van Leeuwen [14] have shown that the presence of a tonic neck reflex may modify the form of a phasic reflex simultaneously elicited, and the interaction of tonic neck and limb reflexes we have described may be an example of such a variation in a phasic reflex (the associated reaction) by a concurrent tonic reflex (the neck reflex). We have only to consider this possibility to dismiss it. As Riddoch and Buzzard have shown, phasic reflexes in the upper limb differ in the quality of the stimulus and in the nature of the response from the associated reactions we have been considering. In every factor concerned, the latter present unmistakably the characters of tonic or postural reactions.

We mentioned earlier a classification of "associated movements" advanced by Marie and Foix, and if we are to orientate the interpretation of these phenomena reached in the present paper, we must consider shortly the views of these observers, whose paper on the subject is at once the most recent and the most comprehensive on the subject. It will be seen that they employ the term "syncinésies" in a much wider sense than that commonly understood by the term "associated movements" in this country. The associated reactions described in Chapter II of the present paper are the "syncinésies globales ou spasmodiques" of Marie and Foix. The second group of these writers is that of "syncinésies d'imitation." These are stated to be rare and of little theoretical importance. They are largely voluntary, and can be inhibited by the subject. They consist in feeble imitative movements in one limb when its fellow carries out rapidly alternating movements. They are to be seen in cases where there is no question of a pyramidal lesion, and occur indifferently in the normal or in the affected hand in such conditions as hemichorea, and hemiathetosis. Marie and Foix consider that they represent an exaggeration of the normal tendency to imitation by the crossed hand or arm of alternating movements. It seems, therefore, that on this definition the movements in question are neither reflex nor tonic, and can be called "associated" only in a loose sense of the word. Under the heading "syncinésies de co-ordination" we find included a somewhat varied collection of motor activities, tonic, phasic, reflex and voluntary, and having for the most part nothing in common. Thus, Magnus and de Kleijn's tonic neck reflexes find a place here, and are stated to be fundamentally distinct from the associated reactions produced by voluntary contraction of muscles. Quite distinct from this group is the phenomenon the description of which follows. A patient with some voluntary control over the affected leg may be unable to dorsiflex the foot as an isolated movement, yet when he is asked to flex the whole limb dorsiflexion of the foot occurs and cannot be inhibited. In these circumstances they regard dorsiflexion as an associated movement. This conclusion seems to embody a conception of the nature of hemiplegia which has not been held in this country since Hughlings Jackson gave us a more profound insight into the matter [2]. We know that isolated movements, especially of the distal segments of the limbs, are the first to suffer in a condition of hemiplegic weakness, while the more deeply organized mass movements of the limbs, which have a complete representation on the reflex levels of the nervous system, are very much more resistant. In every case of residual hemiplegia, we may find abundant illustration of this law of dissolution of function in the nervous system. Therefore, to speak of dorsiflexion of the foot when it occurs as an *integral part of another movement* as an "associated movement" is to stretch the conception of associated movements to a point when it ceases to have any precise meaning. We may conclude, therefore, that interesting as Marie and Foix's classification undoubtedly is, yet it cannot be accepted as based upon a truly scientific analysis.

CHAPTER VI.—CONCLUSIONS.

As the result of a study of the so-called "associated movements" of hemiplegia undertaken during 1912-1914, the general conclusion was reached that they are rather to be regarded as postural reactions, that is, as variations in muscle tone and attitude, than as movements in the strict physiological sense. No precise determination of the factors governing the form of these reactions, nor of their relation to other varieties of tonic reflex reaction, was reached. In the period which has elapsed since these observations were made, there have been striking advances in our knowledge of the nervous processes by which the regulation of tone, that is, the co-ordination of posture, is achieved. The experimental researches of Magnus and de Kleijn and their collaborators must be specially mentioned in this connection, and in the light of this knowledge a re-survey of the problem has been attempted.

It is found that the nature of the adequate stimulus, and the latency, form and duration of these reactions, confirm the view that they are in fact tonic or postural reflex reactions and not "movements" in the strict physiological sense of this term. The adequate stimulus is a tonically maintained voluntary contraction of some part of the skeletal musculature other than the reacting muscles. Forceful tonic contraction of the normal arm is the most powerful stimulus, and no actual excursion or movement is necessary. The response has a characteristically long latent period, in which it differs strikingly from such a phasic reflex as a tendon jerk, is tonically maintained throughout the period of stimulation, develops relatively slowly and as slowly declines, and may show marked tonic after-contraction and "shortening reaction."

When the conditions of investigation are unchanged, the response tends to be invariable in form. The common type consists of increased flexion of the forearm and of the wrist and digits, with variable movement of the shoulder, in which either adduction, abduction or elevation may predominate. In the leg the common response is increased extensor rigidity with some inversion and dorsiflexion of the foot and dorsiflexion of the hallux. Other less common forms are described.

It is found also that not infrequently the "associated reaction," for such it seems more accurate to call it, may be profoundly modified in form by variations in the form of the voluntary contraction eliciting it. Thus, the response to voluntary flexion of the normal arm may be an associated flexion attitude, while on voluntary extension associated extensor spasm may result. On the other hand, reciprocal responses may occur. Such modifications of response are more commonly observed in the upper limb, but are occasionally to be seen in the paralysed leg.

A search for the *tonic neck and labyrinthine reflexes* described by Magnus and de Kleijn was also made, and it was found that, in greater or less facility and intensity, they are almost constantly present in cases of spastic residual hemiplegia. The neck reflexes are the most marked. Rotation of the head so that the face looks towards the paralysed side produces an extensor spasm in the affected arm. In detail, this consists of adduction and advancement of the upper arm, extension and full pronation of the forearm and increased flexion of wrist and digits. Rotation of the head so that the face points towards the normal side produces an attitude of increased flexion in the paralysed arm. In detail this consists either of abduction or of adduction at the shoulder, of increased flexion at the elbow, so that in some instances the clenched fist comes to lie against the front of the shoulder, and of increased flexion of wrist and digits. An influence of the neck reflexes on the lower limb was less frequently observed, but when present obeyed the same laws.

The labyrinthine reflexes, produced by changes in the posture of the head in relation to the horizontal plane, were not so well marked, but in the case of the upper limb evidence was obtained of a reinforcing effect on extensor tonus when the head was placed in the maximal position, that is, with face pointing upwards and the head slightly retracted.

In certain subjects, simple head rotation, or variations in head posture in relation to space, failed to reveal the presence either of neck or of labyrinthine reflexes. In these cases the presence of both could nevertheless be detected when the associated reactions were examined in the prone, supine and lateral positions, and with the head in the median and the two rotated positions. In these various positions the neck and the labyrinthine reflexes combine variously and the resulting reactions are described and analysed.

From all these observations it is concluded that the so-called "associated movements" of hemiplegia are tonic or postural reflex reactions allied to the tonic neck and labyrinthine reflexes of Magnus and de Kleijn. They are best elicited by tonic voluntary activity of the normal limbs, and in these circumstances may be described, following Magnus's nomenclature, as "tonic reflexes arising in the limbs and acting on the limbs." The manner in which they combine and interact with the neck and labyrinthine reflexes confirms the view that they are strictly comparable reactions and belong to a large group of reflex reactions by which muscle tone is regulated and the co-ordination of posture achieved. However, if we consider them as a whole, we find that "associated movements" may result from tonic voluntary contraction in face, neck, trunk and limb muscles and may spread so as to involve all these muscles on the hemiplegic side. While it would be possible to divide these reactions into groups according to their point of origin and seat of response, as indeed we have done in the case of those arising in the limbs and acting on the limbs, no good purpose would be achieved. The point illustrated by associated reactions, whatever their place of origin and seat of response, is that while the tone of a given muscle depends primarily and essentially upon the integrity of its own afferent supply, yet this tone is constantly influenced and modified by impulses arising in proprioceptive end-organs elsewhere in the body. Activated by these deep receptors, the reflex mechanisms situated in the brain-stem achieve the co-ordination of posture. The experimental demonstration of this nervous regulation has been provided by the work of Sherrington, and later and more completely by that of Magnus and his co-workers. In proposing the present interpretation of "associated movements" we are, therefore, simply adding to the already weighty evidence that the processes of reflex co-ordination of movement in man are essentially the same as obtain in the lower mammals, and in man, as in animals, the relative intensity of the various tonic reflexes varies from subject to subject.

In man cortical control of these reflex activities is more complete and far more highly developed, and the lines along which this control has developed are beautifully seen in the records of Sherrington and Leyton's observations on the excitable motor cortex of anthropoids [11]. In hemiplegia this cortical control is more or less completely abolished over the musculature of one half of the body, with the result that there appear on voluntary motor activities two closely allied phenomena, namely, *spasticity* or a selectively distributed hypertonus, and *postural reactions*, including those known clinically as "associated movements." Their "release" from cortical control results not merely in their exaggerated activity, but also and inevitably in their coarse and ill-adapted character. Not only have they been released from control, but they have also depreciated profoundly in fineness of adjustment and purposive adaptation. If, as we believe, spasticity is physiologically identical with experimentally produced decerebrate rigidity, then the appearance of "associated movements" in hemiplegia is a natural corollary to the development of spasticity. Reasons are given for concluding that Marie and Foix's classification of "syncinésies" includes motor phenomena which cannot rightly be termed "associated." Of these some are voluntary, some phasic and only a certain number tonic and reflex in origin. Therefore the term "associated movement," or to be more accurate "associated reaction," should be limited to the phenomena described in Chapter II, it being understood that this is simply an empirical term used to indicate a particular group of postural reflexes, of which allied groups are also present in cases of hemiplegia.

APPENDIX.

The recording kymograph employed is an elaboration of that described and figured in an earlier paper [14], and was made by Messrs. C. F. Palmer, the physiological instrument makers. It consists of a standard Sherrington-Starling drum, mounted on a drum stand fitted with two special upright arms, the one having two light grooved pulleys round which runs a thread carrying a writing point, and terminating in a long spiral spring at one end, and at the other connected with one of the five speeds of a large-coned vulcanite pulley which is fitted to the other upright arm. From the vulcanite pulley another thread leads off to the limb or group of muscles under investigation. The excursion of the writing point may be varied in amplitude, as required, according to the groove selected on the pulley. Other adjustments ensure a suitable tension of the spring, and length of the thread leading to the subject, and allow the taking of two simultaneous records.

A third upright arm carries the signal and the time-recording clock. A drum extension fitting is required for lengthy records. The kymograph is driven by means of a small electric motor.

The graphic recording of reflex movements and postures in man possesses many inherent difficulties. Of these the fixation of the patient during the taking of records is one. Any adventitious change of posture in the trunk, which carries the limb with it, causes an excursion of the writing point and vitiates the record of the movement under investigation. Further, since in many instances an associated flexion of the elbow in the hemiplegic arm is accompanied by adduction or abduction, protraction or retraction at the shoulder, the graphic record is simply an algebraical summation of movements in as many as three planes at once, and is incapable of analysis. Therefore, not every subject is suited for investigation by this method. Those chosen have been subjects in whom the associated reactions were relatively uncomplicated flexion or extension at the elbow or knee, and who could be relied upon to carry out orders accurately and to lie still.

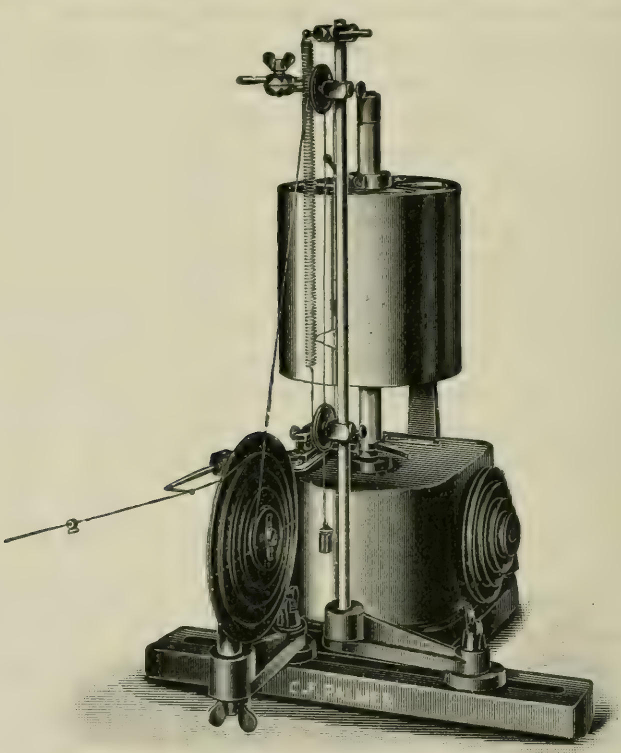


FIG. 11.

The subject lies on his back on a hard couch, the hemiplegic arm from which it is desired to take a record has a bracelet fixed round the wrist and is then slung in such a way that free extension and flexion at the elbow can occur when the muscles go into reflex spasm. The thread is then fixed to the dorsum of the wrist distal to the sling by strapping or some other method.

The signalling of stimulation (head rotation or voluntary grasping) is effected by placing the head or hand in circuit with the signal, so that contact is made only during head movement or during grasping.

ADDENDUM.

While the observations recorded in the foregoing chapters were in process of preparation for publication, the writer's attention was drawn by Professor Magnus in a private communication to the two papers of Simons on the same subject (*Neurologisches Centralblatt*, 1920, 39, 132, and *Zeitschrift für die gesamte Neurologie uud Psychiatrie*, 1923, 80, 499). The latter of these, which contains the full account of Simons' observations, only reached this country when the present paper was completed (March, 1923). It has not, therefore, been possible to do complete justice to Simons' work in the body of the paper. In respect of tonic neck reflexes and their influence on associated reactions it is clear that almost all the observations recorded here have been anticipated by Simons, who has illustrated his work by a series of beautiful photographs. His remarks upon the methods of eliciting tonic neck reflexes, their variations in intensity from day to day in a given subject, and from subject to subject, are in complete accord with the present writer's experience. In respect of the lower limbs, Simons has been able to demonstrate more fully developed neck reflexes than has been found possible from the clinical material available for the present observations. It is clear that cases of cerebral diplegia and of hemiplegia of fairly recent origin in young adults are the material from which the most striking results in this direction are to be anticipated. Simons has not succeeded in demonstrating labyrinthine influence on tone, and concludes that this cannot be revealed in man by the methods adequate for the purpose in the case of animals. Yet it is nowhere clear that he has taken the steps necessary to demonstrate labyrinthine reflexes. He has concerned himself exclusively with the effects on limb tonus and on associated reactions of variations in the relation of the head to the trunk. If the associated reactions be examined with the patient in the supine, prone, right and left lateral positions the influence of the labyrinth can be determined even in the relatively unfavourable clinical material which forms the basis of the present observations. Further, if in each of these four positions head rotation be carried out, it is possible to reveal an interaction of labyrinthine and neck reflexes. On this point, therefore, Simons' work needs amplification.

In addition to the study of neck reflexes in cases presenting pyramidal lesions, Simons has studied a large number of cases presenting one or other of the extrapyramidal syndromes, and has been uniformly unable to demonstrate tonic neck reflexes. The observation is important as emphasizing the fundamental physiological distinction between the spasticity of pyramidal tract lesions and the rigidity of extrapyramidal origin.

He has also been able to demontrate tonic neck reflexes in three cases of high (cervical) spinal lesion. This observation is also of considerable interest. As the present writer has pointed out in the papers referred to in the preceding chapters, the spasticity in the lower limbs in cases of paraplegia in extension is physiologically identical with experimentally produced decerebrate rigidity. It is, however, difficult to understand how a spinal lesion can produce a phenomenon truly akin to this condition. If, as Simons' observations indicate, spinal lesions suffice to produce tonic reflex reactions so closely allied to decerebrate rigidity as are the tonic neck reflexes, then there can be no insuperable obstacle to the view that a form of tonic reflex activity physiologically identical with decerebrate rigidity can result from a lesion at the same anatomical level of the nervous system. It must be stated, however, that Simons does not deal at any length with these or other theoretical considerations, but is primarily concerned to record the facts of observation.

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THE OCULOMOTOR NUCLEUS OF *TARSIUS* AND *NYCTICEBUS*.

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THE researches of Elliot Smith [2] [3] [4] have shown the nature of the cortical changes which are brought about as the result *inter alia* of the enhanced powers of vision developed as a result of the adoption of the arboreal life. He has called attention to the fact that examples of the menotyphlous insectivora lend themselves to comparison as illustrations of these changes, and has described the differences between the brain of the jumping-shrew, *macroscelides*, and the tree-shrew, *tupaia*. "In the tree-shrew," he says, "the importance of the sense of smell is diminished and those of vision, touch, and hearing greatly enhanced. The further emphasizing of these adaptations brought the primates into existence. Among the prosimiæ the reduction of the size of the nose in one group, the tarsioidea, allows the eyes to come to the front of the face so that the fields of vision overlap. The enormous enhancement of the importance of vision which is thus effected leads to the sudden expansion of the cortical area for vision and its further specialization in structure. The sense of sight now completely supplants that of smell as the dominant guide to the animal, and the alteration of the position of the eyes enables the animal to look forward, both in the literal and in the metaphorical senses of the expression" ([4], p. 185).

Brouwer [1], in a clinico-anatomical investigation of the localization of the cell groups comprising the oculomotor nucleus in man, combined with a phylogenetic study embracing representatives of many orders, has been able to deduce certain important principles of general interest relating to the evolution of the oculomotor nucleus. The changes in this structure, it is interesting to note, run parallel with those already referred to in the evolution of the cortex. The most outstanding deduction concerns the relation found to exist between the development of the large-celled median nucleus of Perlia, and the degree of approximation of the two eyes to one another. Brouwer's conclusion is, that these cells appear phylogenetically when the position of the eyes in the head is such as to render convergence possible (op. cit., p. 189). This point is in itself presumptive evidence that this nucleus sends its axones to the internal recti muscles, which effect the convergence developed coincidently with the appearance of the nucleus. Recently Zweig [12] has, by studying other animals than those chosen by Brouwer, confirmed the general truth of this statement.

Brouwer's series suggested further, that the small-celled Edinger-Westphal nucleus, though forming a median cell group in lower forms (e.g., marsupialia, edentata, rodentia, carnivora), becomes split into two nuclei in the anthropoidea.

At the suggestion of Professor Elliot Smith I have recently investigated the relationship of the oculomotor nucleus to the median plane in two important and not distantly related prosimiæ, the spectral tarsier, *Tarsius spectrum*, and the slow loris, *Nycticebus tardigradus*, in order to correlate the structure of the oculomotor nucleus with the cortical development. The material consisted of two specimens of tarsius and one of nycticebus which were stained in paracarmine. One of the tarsius specimens was cut in horizontal serial sections. The remaining tarsius brain-stem and the nycticebus specimen were cut in transverse series. It is a pleasure to record my thanks to Professor Elliot Smith not only for this material, but for the suggestion to undertake the work and for his assistance throughout the research.

The Oculomotor Nucleus of Tarsius spectrum.

As would be expected from an examination of the size of the eyes the visual connections in tarsius are extremely large. Fig. 1 shows the optic chiasma, optic tracts and lateral geniculate body, and the dorsal view (fig. 2) illustrates the enormous size of the superior colliculus.

An examination of the oculomotor nucleus in the sections shows that the large-celled and small-celled moieties may be clearly differentiated the one from the other. The large cells form two prominent groups on each side of the median plane (fig. 3). Lying between these main groups are many large cells situated ventrally, which are scattered over an area including the median plane (figs. 3 and 4). These cells form the central nucleus of Perlia. Though clearly present this group has not the great development found in the higher apes and man, where the Perlia nucleus not only connects together the two lateral nuclei but extends cranially in the median plane between and separate from these groups (c.f. Brouwer's figures reproduced in fig. 7).

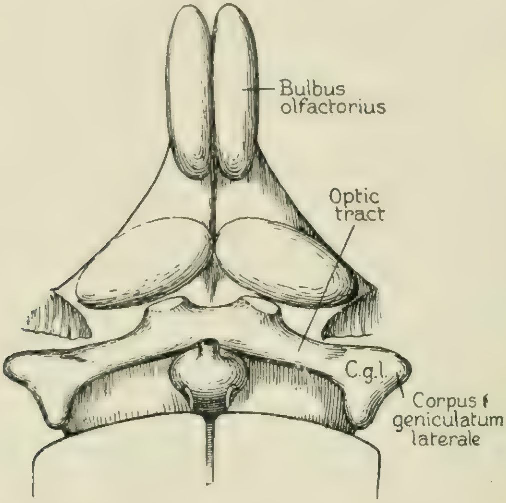

FIG. 1.—Ventral aspect of part of the brain of tarsius.

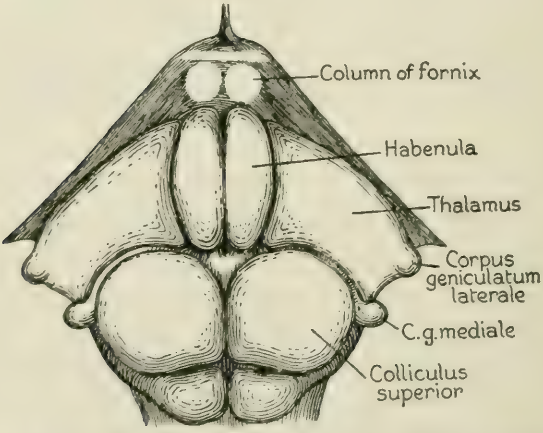

FIG. 2—Dorsal aspect of mid-brain and thalamus of tarsius.

The smaller cells of the oculomotor nucleus form a separate nuclear mass which lies dorsal to the cranial half of the large-celled groups. They stretch across the median plane, so that the division into right and left portions, which is to be seen in the ape and man (fig. 7) is absent in tarsius, although the cells extend to a considerable distance on each side dorsal to the position occupied by the lateral groups of large cells (fig. 3).

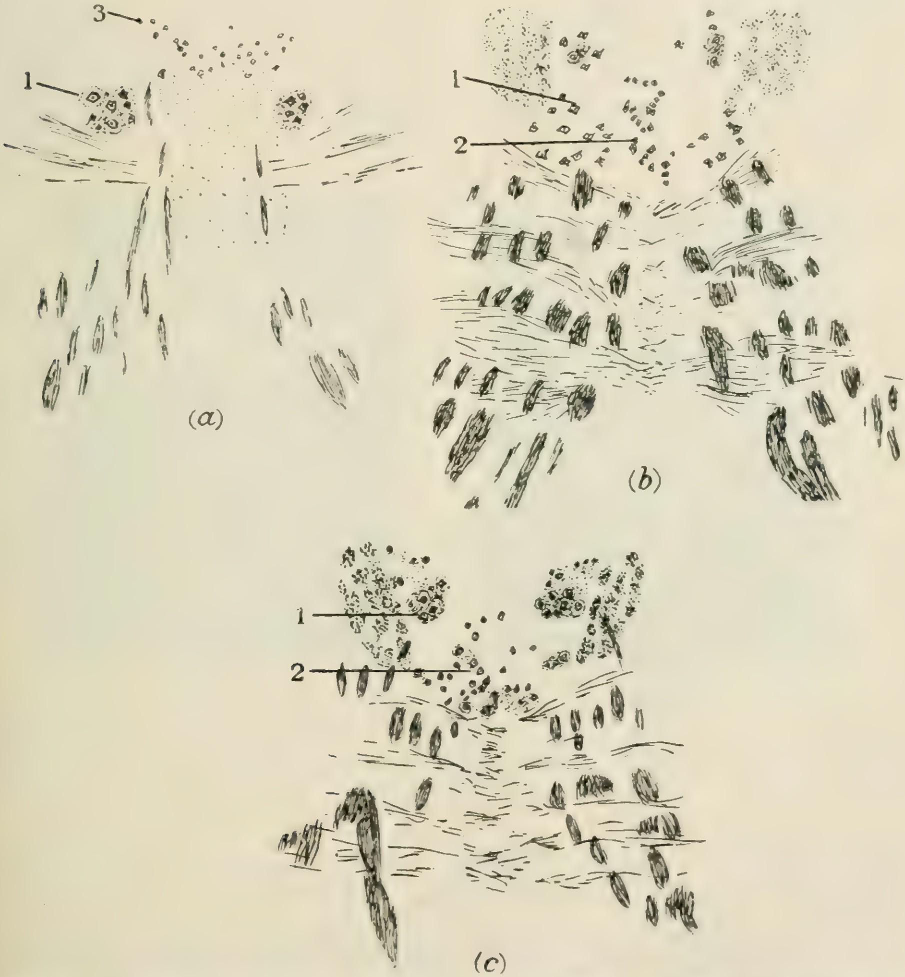

FIG. 3.—Series of transverse sections of oculomotor nucleus of tarsius: (*a*) cranial end; (*b*) middle: (*c*) posterior end. (1, lateral nucleus; 2, nucleus of convergence; 3, Edinger-Westphal nucleus.)

THE OCULOMOTOR NUCLEUS OF NYCTICEBUS.

In this larger brain the relationship of the cell groups to the median plane is revealed with diagrammatic clearness. The large-celled central nucleus of Perlia is beautifully defined (fig. 5).

The relationships of this nucleus are essentially those found in tarsius; it does not attain to the dimensions found in the higher apes and man. The small cells, as in tarsius, here also form a single group which occupies the median line. The illustration (fig. 6) clearly shows

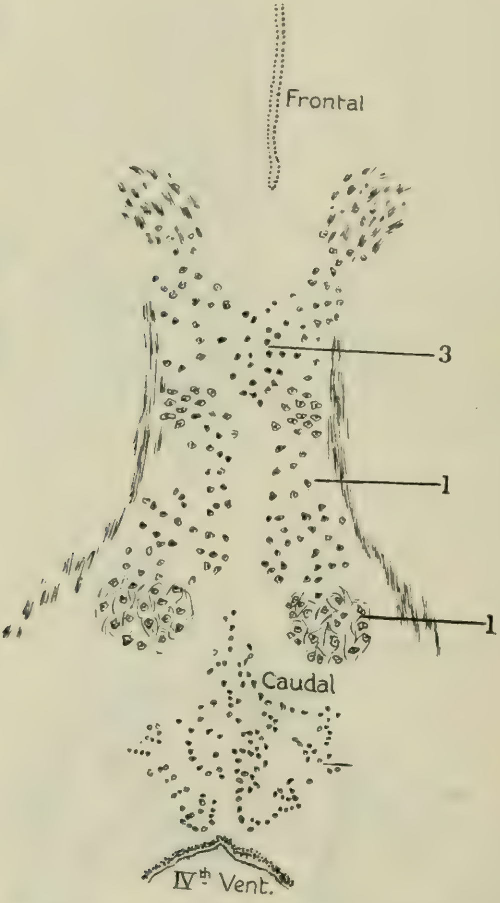

FIG. 4.—Horizontal section of oculomotor nucleus of tarsius. (1, lateral nucleus; 2, nucleus of convergence; 3, Edinger-Westphal nucleus.)

the criteria to be relied upon in the differentiation of these cells from the remaining groups of the oculomotor nucleus. The Edinger-Westphal cells are smaller and less intensely strained than the other cells, and lie closer to the aqueduct of Sylvius (cp. Brouwer, op. cit., p. 171). They are also less distinctly multipolar than the large cells and, as in tarsius, they lie dorsal to the cranial part of the large-celled nucleus.

DISCUSSION.

The reduction of the face has occurred to such an extent in both nycticebus and tarsius that the eyes have become approximated to one another and the fields of vision of the two eyes overlap. This reduction of the face would also render convergence possible, and in support of the contentions of Brouwer the central nucleus of Perlia is to be found in both these forms. The scheme, which has been constructed (fig. 7) to include the oculomotor nucleus of these animals, clearly demonstrates the truth of this relationship. The variations of the small-celled group are also shown in this scheme, but the interpretation of the results presents grave difficulties. The all-important question of the function of this group is still *sub judice*, and is at present the subject of investigation on the part of the Dutch neurological schools. Moreover, Zweig [12] has shown that the grouping of these cells is not so simple as has been supposed. If the view of Bernheimer were correct, that these cells control the ciliary muscle and sphincter action of the pupil, the scheme drawn up would suggest that the grouping of the small cells has a definite relationship to the development of increased powers of accommodation.

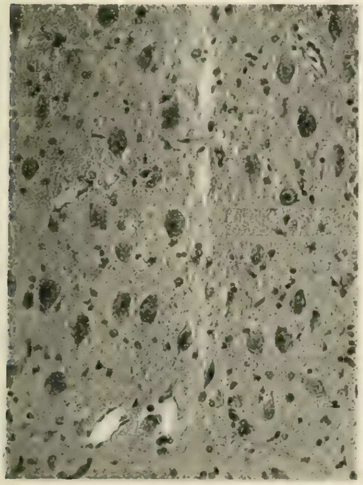

FIG. 5.

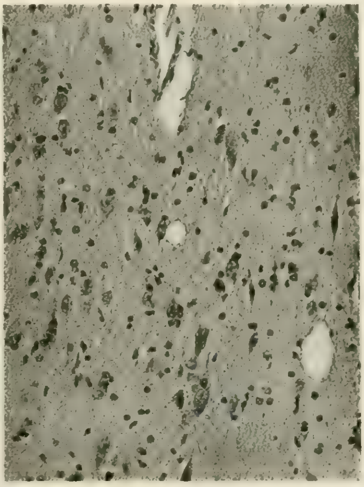

FIG. 6.

FIG. 5.--Photograph of nucleus of Perlia in nycticebus. The slits indicate the median plane.

FIG. 6.—Edinger-Westphal nucleus of nycticebus. The slit indicates the site of the median plane.

In all forms below the monkeys, as the present investigation confirms, the Edinger-Westphal group is a median nucleus. The bilateral arrangement of these small cells in higher forms suggests that the division into right and left parts is to be associated with the development of the power of accommodation of the two eyes so that they may independently focus a given object, even if it is not equidistant from the two eyes, upon corresponding points of the two retinæ. If this explanation proves to be correct as the result of further investigation upon the function of the Edinger-Westphal nucleus, tarsius and nycticebus must be placed below the monkeys in the scheme illustrating phylogenetic phases of development of the oculomotor nucleus (fig. 7). The size of the nucleus of convergence is in harmony with this conclusion, for it is much smaller than is the case in the higher apes and man.

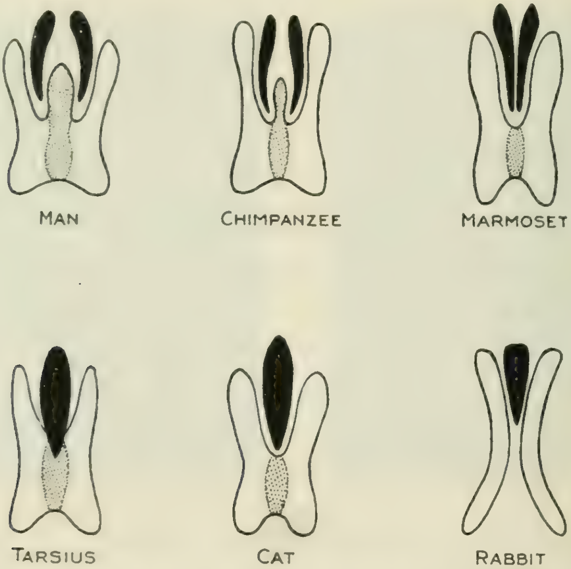

Fig. 7.—Scheme of oculomotor nuclei in various mammals, all except tarsius after Brouwer. Nycticebus would occupy a position immediately below tarsius. (Edinger-Westphal nucleus is represented in black; nucleus of convergence is stippled.)

Fortunately, however, this is not the only evidence which is to be relied upon in this case. In tarsius, in which the visual apparatus has attained a much greater degree of development than in nycticebus, no macula lutea is to be found. Elliot Smith [4] records that Le Gros Clark, while cautiously refraining from denying its presence, has been unable to locate a macula lutea either by the ophthalmoscope in the living animal or by direct examination of the retina after opening the eye in the dead; and also that Woollard has failed to identify it in microscopic preparations. These investigations "make it practically certain that in tarsius the distinctive feature of the retina of the anthropoidea (among mammals) is lacking. In this respect tarsius agrees with the lemurs and differs from all monkeys" (op. cit, p. 185).

Moreover, Woollard in an examination of the optic tract could not find non-decussating fibres (op. cit., p. 185). Only degeneration experiments, which are in this instance impossible to carry out, can provide definite evidence on this point. It is likely, however, from the evidence available, that the crossing fibres are comparatively few compared with their number in higher forms. Wilfred Harris [5] believes that the acquisition of the power of conjugate deviation of the eyes and the development of the semi-decussation of the optic tract synchronize with one another. Examination of the movements of the eyes of animals and an investigation by degeneration methods of the proportion of crossed to direct fibres in the optic tract, has convinced him that the eyes must be yoked together and isolated movements must be in abeyance in order to produce stereoscopic vision. The evidence set forth in this paper shows that changes have been effected in the oculomotor nucleus which are associated with the development of binocular vision. But the structure of the nucleus combined with the evidence recorded regarding the absence of the macula lutea, and the probability that relatively few fibres fail to decussate in the optic chiasma, would suggest that tarsius has not attained the stereoscopic vision which is possessed by apes and man. This conclusion harmonizes with that of Treacher Collins [9], who in his Bowman Lecture points out that "no mammals below monkeys have a capacity of distinguishing detail such as is associated with the presence of a fovea centralis," although there is evidence to show "that in the carnivora there is an area centralis in the retina more acutely sensitive to form than the periphery" (p. 29). In summarizing the stages of progressive development of binocular vision, Parsons [7] refers to the evidence of Harris (op. cit.) on this point, and concludes that it seems probable that the cat has stereoscopic vision, and that this is associated with the prehension of the prey by the fore-limbs" (p. 107). Be that as it may, there can be no doubt that in monkeys, as Parsons also states, a distinct advance is made on lower forms, as is shown by the greater range and variety of conjugate movements of the eye and by the development of a true fovea. It is certain that this stage of development is not attained by tarsius and nycticebus.

It is interesting to note that Riddoch [8] has brought forward clinical evidence which illustrates the true nature of stereoscopic as compared with binocular vision. Riddoch's patient was unable to localize the distance of an object from him, and he could not appreciate the depth and thickness of objects notwithstanding a perfect consciousness of light and shade (p. 47). Riddoch (op. cit., p. 18) has also shown that in recovery of vision after occipital lobe lesions perception of movement precedes that of the moving object, and that the recovery of movement vision begins at the periphery. These conditions probably represent reversions to phylogenetic phases in the evolution of visual perception. The phases of development have been called panoramic, binocular, and stereoscopic respectively; but it must always be borne in mind that one merges into the other. In the transition from panoramic to binocular vision recession of the face with consequent development of the power of convergence is the main factor. The attainment of stereoscopic vision is accompanied by the development of an increased range and variety of the conjugate movement of the eyes, and by the development of a macula lutea in which each foveal cone becomes connected with a single bipolar cell which raises discriminative capacity (Parsons, p. 109). It must not be forgotten that the increased usefulness of the hands would contribute materially to visual experience in regard to the estimation of size and shape. Moreover increased skill in handling small objects must be accompanied by the development of considerable acuity of vision. Nycticebus, like the lemurs (Treacher Collins, op. cit., p. 43), has probably not developed a fovea centralis because it makes use of its mouth in grasping its food to a much greater extent than monkeys (Wood Jones [10], p. 87), or perhaps it would be more logically expressed by the statement that it uses its mouth because it has not yet acquired sufficiently exact visual control to guide its hands with precision. Tarsius makes more use of its hands, but the lack of extensive conjugate movements of the eyes has to a considerable extent been made good by the increased range of movement of the head. This substitution of a gross movement of the eyes and head for the delicately co-ordinated conjugate movements of the eyeballs has probably been a factor in retarding the development of acute form-sense in tarsius. In other respects tarsius exhibits "an over-development of and an exaggerated reliance upon those specializations of vision and its cerebral instruments which were responsible for the differentiation of the tarsioidea from the lemuroidea and gave impetus to those developments which produced the anthropoidea from one of the tarsioid families" (Elliot Smith [3], p. 466). In becoming a nocturnal animal to secure its safety tarsius lost all opportunity of developing the specialized area at the fovea consisting of a close congregation of cones, the threshold response of which is high. It seems probable that the central stock leading to the anthropoidea attained its supremacy because, as the nose receded and binocular vision with convergence was developed, it acquired synchronously and in due proportion movements of the head and conjugate movements of the eyes (to increase the range of vision which would otherwise be less in the binocular than in the panoramic stage), and an increased range of movement of the fore-limbs.

SUMMARY.

The oculomotor nuclei of *Tarsius spectrum* and *Nycticebus tardigradus* exhibit the presence of a central nucleus of Perlia which is smaller than in the anthropoidea. The presence of this nucleus in these forms accords with the conclusion of Brouwer that the median large-celled nucleus appears phylogentically when the recession of the face allows the approximation and consequent convergence of the eyes. The Edinger-Westphal nucleus is in each case a single nucleus lying dorsal to the large-celled groups in the median plane and extending laterally from it. In the anthropoidea this nucleus is bilateral (Brouwer), and following Bernheimer's theory as to the function of these cells, it is suggested that the power of independently focusing an object on corresponding points of the retinæ, although the object is not equidistant from the two eyes, is to be associated with this bilateral arrangement. The evidence to show that a macula lutea is absent in tarsius is set forth (Elliot Smith, Le Gros Clark, Woollard), and it is also concluded that relatively few optic fibres fail to cross in the optic chiasma. These differences from the anthropoidea are believed to indicate the possession by tarsius of a less acute form sense than in higher forms, i.e., stereoscopic vision has not yet been properly attained.

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LETHARGIC ENCEPHALITIS AND HERPES FEBRILIS.

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INTRODUCTION.

THE nature of the infecting agent in encephalitis lethargica is still a matter of interest, though much work has been done towards the solution of the problem

These investigations have also thrown considerable light on the ætiology of many other infectious diseases.

The first researches on the ætiology of encephalitis lethargica (Wiesner, Bernhard) are now of historical interest only. They attributed it to the virus of influenza, especially the polymorphous diplostreptococcus. It was proved afterwards that the ætiology of these two diseases is different, and that this micro-organism is found in mixed infections only. Wiesner inoculated a monkey with positive result, but it was due to an acute non-specific infection.

Strauss, Hirschfeld and Loewe undertook research work on a larger scale. They inoculated monkeys and rabbits intracerebrally, using the emulsified brain substance from fatal cases of the disease, the discharge from the nasopharynx, and the cerebrospinal fluid. They produced constant and specific lesions in the brain, and they also found this infective when injected into other animals. By this means they were able to get a series of passages. Bacteriological examination did not reveal any micro-organism, and the brain emulsion did not lose its virulence by passing through a porcelain filter. They thus discovered that the virus is a filtrable one, and belongs to the ultramicroscopic group. They succeeded later in growing, under anaerobic conditions on a transudate, very small round bodies which stained with the greatest difficulty by Giemsa stain. These when injected into a rabbit caused a specific infection; with these cultures they obtained a high percentage of positive results.

European investigators have been less fortunate, but McIntosh and Turnbull inoculated a monkey subdurally with an infected brain emulsion with a positive result; when the monkey died two months later there were typical changes in its nervous system.

The experimental difficulties in research work on this subject were first shown by Levaditi [2]. He made thirty inoculations into the brain and peritoneum of nineteen rabbits, thirteen monkeys and eight guinea-pigs. The infecting material was taken from sixteen cases proved clinically and by microscopic examination to suffer from the disease. Brain emulsion was inoculated ten times, blood three times, cerebrospinal fluid twice, saliva once and discharge from the nasopharynx once. The whole series of experiments produced only two positive results and one doubtful one. Levaditi concluded that it was difficult to reproduce the disease of the Paris epidemic of 1919-20 by inoculation into the rabbit and monkey, and that the virus was located in the nervous system.

Doerr [1] was unsuccessful in his first experiments. The infecting material from eleven cases was inoculated into sixteen rabbits, four guinea-pigs, two mice and five cats without any result. Only the twelfth experiment, in which the cerebrospinal fluid was inoculated into a rabbit under the dura mater, gave a positive result.

Kling in Sweden and Ottolenghi in Italy worked on a much smaller scale. They confirmed the researches of Levaditi. Doerr and all other authors agree that the virus of lethargic encephalitis is a filtrable one, and that all attempts at culture have been hitherto unsuccessful.

The virus is inoculable in laboratory animals, especially monkeys and rabbits, not always with the same ease. In some epidemics a higher percentage of positive results is obtained than in others. This is proved by the different rate of mortality and the clinical symptoms of the infected animals, as we shall see in the second part of this paper. The specific pathological lesions are found in all the inoculated animals. The virus is easily preserved in glycerin, but is destroyed by bile, disinfectants and by heating. The result of inoculation depends on the route by which the infected material is introduced; the best method is inoculation into the cornea or under the dura mater. Intravenous, intraperitoneal and subcutaneous inoculations generally give negative results.

It is a curious fact that inoculation into the testicle causes no local changes here, although the virus remains potent for some time (Levaditi).

From our researches we have come to the same conclusions as Levaditi and Doerr. No matter in what way the virus is introduced into the animal, it always becomes localized in the central nervous system, travelling to it along the nerve trunks. This was proved by Levaditi, who inoculated a rabbit in the eye; twenty-four hours after inoculation the optic nerve was found to be infected, though the watery discharge from the eye was already sterile. The blood and internal organs do not contain the virus, except the liver where we found specific changes, but our work on this matter is not yet completed.

Important contributions to the ætiology of encephalitis lethargica have been made by researches on herpes febrilis. These were begun by Loewenstern in 1914, continued by Blanc and his fellow workers, and by Doerr and Levaditi. The results of their work may be briefly summarized as follows:—

The vesicles of herpes febrilis contain a filtrable virus, infectious to the rabbit and in a lesser degree to the guinea-pig and mouse. Scratching the cornea of a rabbit with a scalpel infected with the contents of a herpetic vesicle produces along the scratch a series of typical vesicles, accompanied by a conjunctivitis and a thick profuse discharge. According to the intensity of the inflammation this may result in a slight opacity of the cornea, or in the loss of the eye. The virus can be transferred from cornea to cornea. No other micro-organisms are found in the discharge from the conjunctival sac. The diluted discharge passed through a porcelain filter retains its infectivity, and when inoculated into the brain of a rabbit it produces all the symptoms of lethargic encephalitis and leads invariably to the death of the animal. Its virulence can be kept up through a series of passages. It is an interesting fact that the contents of herpetic vesicles occurring in various febrile diseases, as herpes genitalis and herpes zoster, produce the same changes in the rabbit. Consequently the viruses of encephalitis lethargica and of herpes febrilis are closely related, if not identical. The contents of a herpetic vesicle introduced under the dura mater cause specific changes in the brain, and a brain emulsion from an infected rabbit produces identical changes in the cornea. In both instances a series of passages is easily obtained. The brain of a rabbit infected from a herpetic vesicle retains its virulence when preserved in glycerin, but this is destroyed by carbolic acid and bile, and by heat. Reciprocal immunity was obtained with both viruses, inoculation of the cornea with the contents of a vesicle from febrile herpes making the rabbit immune to an intradural inoculation of the virus of encephalitis lethargica, and vice versa.

The close relation of these viruses to each other is shown by the result of inoculation of a rabbit with the saliva of a patient convalescent from encephalitis lethargica. Levaditi found that this produces typical changes in the rabbit. Later, however, it was discovered that the saliva of fifty per cent. of normal people is capable of producing the same changes. A rabbit inoculated with the saliva becomes immune to the inoculation of the virus of encephalitis lethargica.

From these facts Levaditi draws far-going conclusions. He considers that persons capable of infecting rabbits with their saliva are carriers of encephalitis lethargica, or convalescent from it.

Doerr takes a much simpler view; he believes that normal human saliva may contain the virus of herpes febrilis, and that when this is so the persons are carriers of the herpetic not of the encephalitic virus.

In spite of difference in the interpretation of certain points different observers on the whole agree on the fundamental facts. They agree that there exists a virus or a series of viruses closely related to one another, the inoculation of which causes identical changes in the rabbit. They are all filtrable, easily preserved in glycerin, easily destroyed by bile and other agents, show a special affinity for the brain and skin, and are able to produce cross-immunity.

It is curious that these two viruses so closely related to each other show such a great difference in affecting man, sometimes producing encephalitis lethargica, more often herpes febrilis. Doerr thinks that this may be due to a difference in virulence.

Levaditi has attempted to classify these filtrable viruses with a special affinity to tissues of ectodermal origin, especially to the brain, as ectodermic neurotropes. The viruses of rabies, small-pox and acute poliomyelitis probably belong to this group. They differ from each other by the symptoms they produce, which depends on the ectodermal tissue they affect. Their common characteristic lies in their affinity for these tissues only.

It has been shown that the small-pox virus when inoculated subdurally invariably causes death of the animal. By a series of passages its virulence can be increased, till such a virus is still active in dilution of 1 in 1,000,000 after passages extending over nine months (Levaditi). The virus also gives a definite tissue-immunity when inoculated into the rabbit in very small amounts. The blood of the inoculated animal contains no substance that can neutralize the virus, but its brain when mixed with the virus neutralizes it. The brain of an immunized rabbit inoculated with the small-pox speedily destroys the virus; two hours later the brain contains no trace of the virus, but the brain of a normal rabbit inoculated with the same small-pox virus becomes virulent after twenty-four hours, that is to say, twenty-four hours is required for the virus to develop in the brain of a rabbit. These facts are probably true for the whole group, to which belong the virus of normal saliva that produces specific infections when inoculated into the cornea, the virus of herpes febrilis and that of encephalitis lethargica. The virus of small-pox causes changes in the skin and the cornea, and affects the brain and spinal cord too. That of rabies produces no specific changes in the skin, and when inoculated into the cornea excites no local changes but becomes localized in the brain and spinal cord. The virus of acute poliomyelitis cannot be inoculated through the skin or cornea, and it produces much slighter changes in the mid-brain and hemispheres than in the spinal cord.

There are other infections in man and animals related to herpes febrilis and encephalitis lethargica, the causal agents of which are unknown. As an example we may mention chicken-pox. There are clinical observations which show the possibility of a chicken-pox epidemic originating from a case of herpes febrilis, and certain experiments prove that the cornea of a rabbit may be infected by the contents of the chicken-pox vesicles. We know very little of the ætiology of mumps, but Levaditi thinks its virus may be closely related to that of lethargic encephalitis. Foot-and-mouth disease, in which the lesions are limited to tissues of ectodermal origin and very similar to those of herpes, and the so-called "Bornasche-Krankheit" of horses which resembles encephalitis lethargica, also belong to the same group.

There are a few points of theoretical interest to which we would like to call attention. Calmette and Guerin found that if one side of a rabbit be shaved and the small-pox virus introduced intravenously, only the shaved side develops the disease. The cause of this is unknown; according to Levaditi there is after shaving an intense proliferation of the superficial layers of the skin in the neighbourhood of the hair follicles, and these young proliferating epithelial cells are a suitable soil on which the small-pox virus may develop. It was shown later that small-pox develops easily on young tissues of ectodermal origin, as cancerous growths of mice and infectious epithelial tumours of fowls.

The ætiology of herpes febrilis, in the light of these new investigations, seemed to us important enough to warrant further experimental investigation.

Herpes febrilis until lately was regarded as an innocent infection of the skin, appearing either by itself or associated with some acute or chronic infectious disease, as pneumonia, acute cerebrospinal fever or tabes dorsalis, but we know now that it is capable of affecting seriously the nervous system of the rabbit and leading to its death. Our aim has been to determine exactly the pathological and topographical changes caused by the infection. We have also tried to produce in rabbits encephalitis lethargica in order to compare, from the clinical and anatomical points of view, the changes caused by it with those due to herpes febrilis.

ENCEPHALITIS HERPETICA.

The infecting material was obtained from idiopathic herpes and from herpes associated with cerebrospinal fever and scrofulosis. The inoculations were made through the eye, the cornea being lightly scratched, as in vaccination, with a scalpel. The skin of the patient suffering from herpes was cleaned with ether, the vesicles pricked and the infective material carried by the scalpel to the damaged cornea and rubbed in with some flat instrument. Some of the infective material was often left in the conjunctival sac. All the experiments gave positive results. As a rule, on the third day the cornea became opaque and a thick white purulent discharge poured from the eye. The course of the disease was either acute or chronic.

Acute form.—The general symptoms develop five or seven days after inoculation and death supervenes within a few hours.

Rabbit No. 9, inoculated on March 3, 1922, in the left eye with the contents of a vesicle of herpes febrilis from a case of cerebrospinal fever. On the third day there was a thick purulent discharge from the left eye and some from the right eye too. A week later the animal died in convulsions with typical circus movements.

In the *chronic form* the symptoms develop slowly. The local eye changes diminish gradually and after a few days the animal recovers completely or almost so, but some time later the symptoms reappear.

Rabbit No. 1, inoculated into both eyes December 3, 1921, with the contents of a herpetic vesicle from the ear of a tubercular child; three days later vesicles developed on both eyes, the conjunctivæ were swollen and a thick purulent discharge poured from both eyes, the bacteriological examination of which proved negative. On December 20 both cornea were opaque but there were no vesicles. The left fore limb was paretic and in running the animal deviated towards the right. Those symptoms disappeared and the rabbit seemed well until the middle of January, 1922. Its temperature was not raised. On January 15 temperature rose to 38°; the head was turned to the right, with the occiput towards the left shoulder, and this forced position persisted in spite of correction. The position of trunk and limbs at rest was normal. In running the limbs were set widely apart, the animal deviated towards the right, fell on its flank and rotated on its longitudinal axis. Placed on its legs the head oscillated in the antero-posterior plane, and there was a vertical nystagmus of the eyes. It frequently ran about with the left side of the muzzle touching the floor, and the right side turned upwards. This condition persisted for two weeks. It was then killed by a blow on the back. An emulsion of its brain was inoculated into another rabbit.

In the chronic cases the animal often dies without apparent cause.

Rabbit No. 5, inoculated on February 7, 1922, with the contents of a herpetic vesicle from a case of cerebrospinal fever, did not show any general signs, but the local changes in the eye were typical of herpetic infection. The animal died on March 3, 1922. Its brain showed typical anatomical lesions of the ordinary distribution.

Inoculation under the dura mater.—The same clinical picture is obtained by subdural inoculations: 1 grm. of brain-tissue from the mid-brain of an animal dead of the disease was emulsified in 5 grm. of normal saline and 0·3 grm. injected subdurally.

Rabbit No. 4 was inoculated under the dura mater with a brain emulsion of rabbit No. 3 on January 25, 1922. General symptoms, as stiffness of the jaw, salivation, circus movements and convulsions, appeared six days later and death occurred on the same day.

These experiments show that herpes, whether idiopathic or complicating cerebrospinal fever, is an infectious disease capable of being transmitted by corneal or subdural inoculations to the central nervous system of rabbits, and the brain of an inoculated animal is infective to other animals. The cerebral changes are manifested clinically by a series of nervous symptoms, as unnatural positions of the head, stereotyped circus movements of the body, profuse salivation, stiffness of the jaw, convulsions and paresis. Post-mortem examination of the brain always reveals pathological changes, which, as we will see in the second part of our work, are identical with those due to encephalitis lethargica.

In our researches we have dealt only with idiopathic herpes, and with herpes complicating cerebrospinal fever and scrofulosis. According to Levaditi and Lipschütz, the same results are obtained with herpes complicating pneumonia and herpes zoster. Until now it has been thought that herpes febrilis was a special reaction of the skin to different infections, and not a disease *sui generis*; that occurring in cerebrospinal fever has been attributed to the meningococcus, which some observers claim to have demonstrated in the vesicles. Recent investigations must make us revise this hypothesis.

One of us was able to observe two cases which throw some light on the question. One patient, a boy aged 7 years, presented all the signs of cerebrospinal fever. viz., headache. vomiting, stiff neck, dilated pupils, Kernig's sign, high temperature with remissions during the day, and a profuse herpetic eruption beginning on the third day of the disease. A lumbar puncture did not, however, confirm the diagnosis. No other disease was found in the internal organs. Seven days later the boy recovered. In this case the general symptoms seem to have been due to the herpetic infection. The other case was a woman, aged 30, who came to the out-patient department complaining of intense headache, vomiting, sore throat and shivering, of three days' duration. On the second day of the disease she complained of giddiness and felt sleepy. Clinical examination revealed a sore throat, enlarged tonsils and a profuse herpetic eruption on the lips, which, according to the patient, appeared on the third day of the disease. The course of the disease was benign. It seems to us that the sleepiness, vomiting and giddiness were not simple manifestations of the angina, and that the herpetic eruption played here an important rôle.

We find in the literature descriptions of febris herpetica which differ from our cases in the fact that the eruption appeared after the fall of the temperature.

Our researches on encephalitis lethargica confirm, on the whole, the observations of Levaditi and Doerr, with some slight differences. Doerr thinks that animals inoculated through the cornea develop the disease more slowly and die two to four days after the appearance of the first symptom, while in animals inoculated under the dura mater death occurs in twenty-four to thirty-six hours after the appearance of symptoms. This statement was not confirmed by us. We did not find any difference in the clinical course of the disease in animals inoculated through the cornea or subdurally. The susceptibility of the animal seems to be more important; in small animals and albinos the disease often runs a very acute course.

Rabbit No. 6, an albino, 600 grm. in weight, was inoculated on March 11, 1922, under the dura mater with a brain emulsion of rabbit No. 2, which had been infected with the contents of a herpetic vesicle by the cornea. It died on the third day without showing symptoms. The post-mortem examination showed typical changes in the brain, from which we concluded that death was due to the specific infection.

ENCEPHALITIS LETHARGICA (EPIDEMICA).

We employed as infective material cerebrospinal fluid and discharge from the nasopharynx of cases suffering with encephalitis lethargica, and emulsions of the brains of patients dead of this disease. The infective material was introduced into the eye, and under the dura mater of the brain or of the spinal cord.

Fifty-five inoculations gave eighteen positive results (33 per cent.); that is to say, these animals developed clinical symptoms and died. With the cerebrospinal fluid of one case twelve rabbits were inoculated.

The patient, a man, aged 48 years, became ill in April, 1922. At first he complained of general malaise and anorexia. On the third day myoclonic movements of the lips and lower limbs developed. He became excited and anxious, and on the sixth day sleepless by night and day. Bowels and bladder acted with difficulty. He was admitted into hospital on the tenth day of the illness. There was ptosis of both eyes, more marked on the right side; the reactions of the pupils to light and accommodation were diminished, the ocular movements were limited and the patient was excited and wandered. Occasionally he could be roused and then seemed more conscious of his surroundings, but he was less oriented as regards time. His face was mask-like, skin glossy, and there were myoclonic movements of his lips, nostrils and neck. Temperature was slightly raised, pulse 120, respiration 42. Urine contained 0·2 per cent. of albumin. The cerebrospinal fluid was clear, globulin reaction negative, but the Pandy, Weichbrodt and Targowla reactions were positive; albumin 0·16 per cent., sugar 0·7 per cent., and 16 cells per 1 c.mm.

Rabbits 21a and 21b were inoculated in the usual manner into the cornea with the cerebrospinal fluid of this patient, and on the following day the second eye of each rabbit was inoculated with discharge from his nasopharynx. Three weeks later both rabbits appeared quite well, their temperatures were normal and no changes developed in the eyes, except a small white spot on the left eye of rabbit 21a, which had been infected with the nasopharyngeal discharge. On May 15, twenty-six days after inoculation, rabbit 21a showed definite symptoms, as retraction of the head, profuse salivation and seizures in which the hind limbs were extended and the fore limbs and the muscles of the muzzle convulsed. These attacks usually lasted a few minutes and after them the animal ran about in circus movements to the left. Between the attacks the animal seemed dazed, and when immobile stood with its fore limbs widely apart. When running in a straight line it failed to avoid obstacles, and often hurt its muzzle against the wall. The animal died eighteen hours later. Macroscopically the brain showed some congestion, and microscopically marked inflammatory and degenerative changes, which will be described later, were found in it.

After the death of this patient a brain emulsion of the grey matter of the mid-brain, obtained under strict aseptic conditions, was inoculated into the cornea and under the dura mater of six rabbits. Five animals died, one four days after the inoculation without showing any clinical symptoms. Rabbit No. 25 died two weeks after the inoculation under the dura mater For twelve days it seemed well, but then the temperature rose to 39° for three days, and the animal became dazed, immobile, and lay with its back arched. Three days later the temperature fell to 35° and the animal died. Rabbits 21 and 26 died three weeks later without developing clinical symptoms, and the fifth rabbit died a month after inoculation without clinical symptoms too. In all five rabbits there was marked meningitis and inflammation of the nervous tissues. The sixth rabbit remained well, but when killed six months later its nervous system showed marked inflammatory scarring, which will be described later.

This group of observations shows how very difficult it is to determine the inoculation period, and even to prove clinically that the infection had taken place. The disease may run a most acute course to a fatal termination within four days, or may end in recovery after a protracted course. It may be said that on the whole the acute form lasts two weeks, the chronic form four to six weeks, both terminating fatally. As in the herpetic infections, small sized animals are more susceptible, the disease being more acute in them. The site of inoculation does not seem to have an important influence on the course of the disease: rabbit No. 23 died four days after the inoculation into the eye ; all the other animals were inoculated under the dura mater.

In another series of experiments the cerebrospinal fluid of a woman, aged 42, was used as inoculation material.

On April 10, 1922, she complained of dimness of vision and sleepiness. When awake she was quite conscious. Two weeks later she became sleepless ; during the whole time she did not complain of pain. At the beginning of May she developed myoclonic movements in her left upper limb. When she was admitted to hospital on May 10 her eyes were half-closed, the ocular movements were normal, and there was no nystagmus ; the pupils unequal, the right being larger, their reaction to light was diminished and that to accommodation lost. There were incessant movements of the fingers of the left upper limb which took the form of scratching the inner side of the thumb or the thenar eminence; sometimes she scratched her head in the same stereotyped way. Those movements ceased during sleep. In the lower limbs there was constant dorsiflexion and extension of both feet, and from time to time slight raising of the whole limb. The tendon reflexes were lively, the skin reflexes diminished. The tension of the muscles at the left elbow was slightly increased (slight stiffness on extension of the joint). The cerebrospinal fluid was clear but under slight tension; the Nonne-Apelt reaction was slightly positive but there was no excess of cells.

0·5 c.cm. of the fluid was injected into two rabbits.

Rabbit No. 34 was inoculated under the dura mater and into the spinal canal; rabbit No. 36 into the right eye. The first rabbit died three and a half months after the inoculation, the second four weeks after it. The first one was a big specimen, the second of small size.

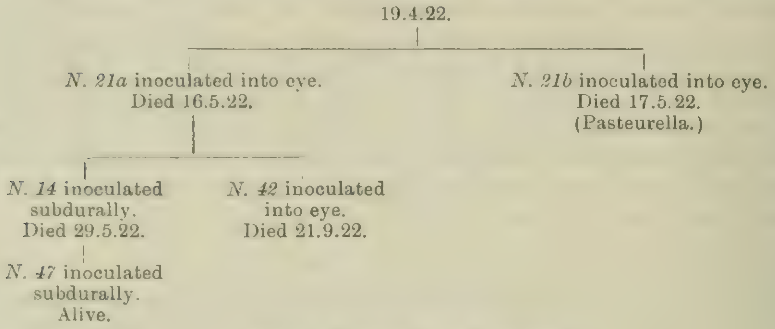
Five days after inoculation rabbit No. 36 showed a slight paresis of the right hind leg, which passed off in a few days. Two weeks later the temperature rose to 40° for a week or so, but dropped to 36° before death. For one day before its death rabbit No. 34 seemed dazed, reeled to the left when running, had marked head retraction and trembled all over.

In a series of inoculations with infective material from other patients the results were much the same. The results were equally positive with inoculations of cerebrospinal fluid, of the discharge from the nasopharynx and of brain emulsion. Anatomical changes were found in all, but clinical symptoms in a certain proportion only. We also noticed that the virulence of the infective material depended less on its source than on the intensity of the disease in the patient.

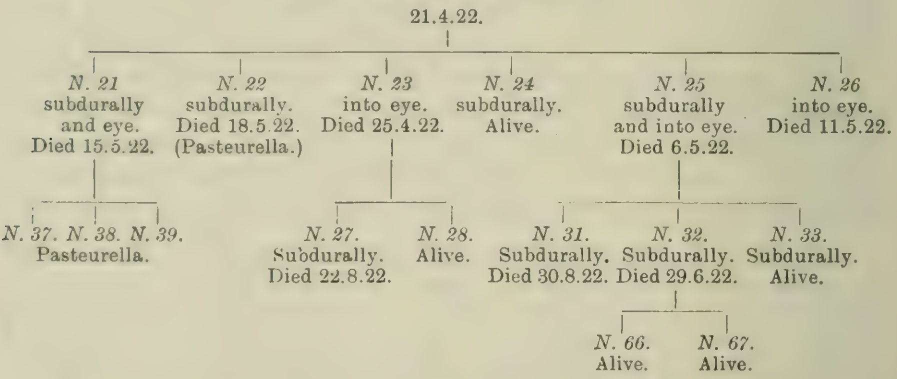
Inoculation of Healthy Rabbits with Brain Emulsions of Rabbits infected with Encephalitis Lethargica.

In this series of experiments we inoculated animals with brain emulsions from other animals who had died from the disease, or had been killed after infection. We are unable to classify the results of these experiments since a secondary infection (pasteurella) destroyed a great number of our animals. We counted only those cases as positive which showed clinical symptoms typical of the disease, and which were free from the pasteurella infection. It is much more difficult to infect rabbits with material taken from other infected rabbits than with material from human patients. The following charts illustrate this clearly.

CEREBROSPINAL FLUID AND DISCHARGE FROM NASOPHARYNX OF PATIENT C.



BRAIN EMULSION OF PATIENT C.



The incubation period is prolonged when the infection is transferred from animal to animal; as an example we may mention rabbit No. 31 which, inoculated subdurally and into the right eye on May 6, with a brain emulsion of rabbit No. 25, remained quite well for four months, during which time there were no signs that infection had taken place. Then the temperature rose to 39·6°, the head turned to the left and downwards, the animal lay on his left flank and when put on his legs executed definite circus movements, the left legs moving on the smaller curve. It frequently rotated on its longitudinal axis, the right side turning round to the left. There was vertical nystagmus, more marked in the right eye. When held up by its ears the body and hind limbs described circular movements in the air and when placed again on the floor oscillatory movements of the head appeared. These symptoms lasted two days. The animal was killed by a blow on the head. Rabbit No. 42, infected with a brain emulsion of rabbit No. 21a, had also a long incubation period (see diagram). There was a slight ulceration on the right cornea and a slight rise of temperature. The animal died four months later. Its brain showed typical changes. As an example of a more acute course in the same series we may mention rabbit No. 41, which was inoculated subdurally on May 16 with a brain emulsion of rabbit 21a; six days later the temperature rose to 40·8° and the hind legs became paralysed. During the next six days the temperature fell to 36° and the animal died on May 29.

We must therefore conclude that the clinical symptoms of infection by encephalitis lethargica are identical with those of herpetic infection. The local changes in the eyes are, however, much more intense in the herpetic infection; in encephalitis lethargica there may be no reaction, or a slight irritation of the eyes only. Levaditi believes this is due to the greater affinity of the herpetic virus for the skin and designates this property dermotropic; he terms the affinity of the virus of encephalitis lethargica for the brain tissue neurotropic.

There is a great difference between the clinical course of the disease in man and in animals. In the latter the infection is not always accompanied by clinical symptoms and is sometimes detected only by post-mortem examination. It is not known that in man symptoms may be absent when infection is present.

In animals the most common symptoms are abnormal positions of the head, circus movements, nystagmus and oscillatory movements of the head, that is, symptoms of labyrinthine involvement. Siegrist and Stocker have, in fact, observed involvement of the labyrinth and thought it was the cause of the symptoms. Doerr and Schnabel found the same symptoms in animals whether the labyrinths were involved or not. In our series no involvement of the labyrinth was found in the pathological examinations made by Dr. Karbowski. We therefore attribute the symptoms to involvement of the nervous system, and indeed we always found there changes capable of explaining them. Another frequent symptom in animals which is seldom found in man are either general or local convulsions.

We certainly do not agree with Kling, David and Lilienquist, who describe a great similarity between the symptoms in man and animals, these being "spasmodic or catatonic conditions, tremors not unlike the tremor of Parkinson's disease, and convulsions." We never noticed in our series such spasmodic or catatonic symptoms, nor tremor nor myoclonic movements, and convulsions occur very rarely in man.

Symptoms of Parkinson's disease appear in man later, when the disease has lasted for some time. We purposely kept a certain number of rabbits alive in order to see if this complication would arise, but it has not occurred till now. We have also failed to observe in our rabbits any sleepiness or paralysis of the oculo-motor nerves. We do not think that running into obstacles was due to visual troubles as Doerr and Schnabel believe; examination of vision and histological examination of the nervous system do not support their view. It was more probably due to the kinetic and static disturbances so frequent in our animals.

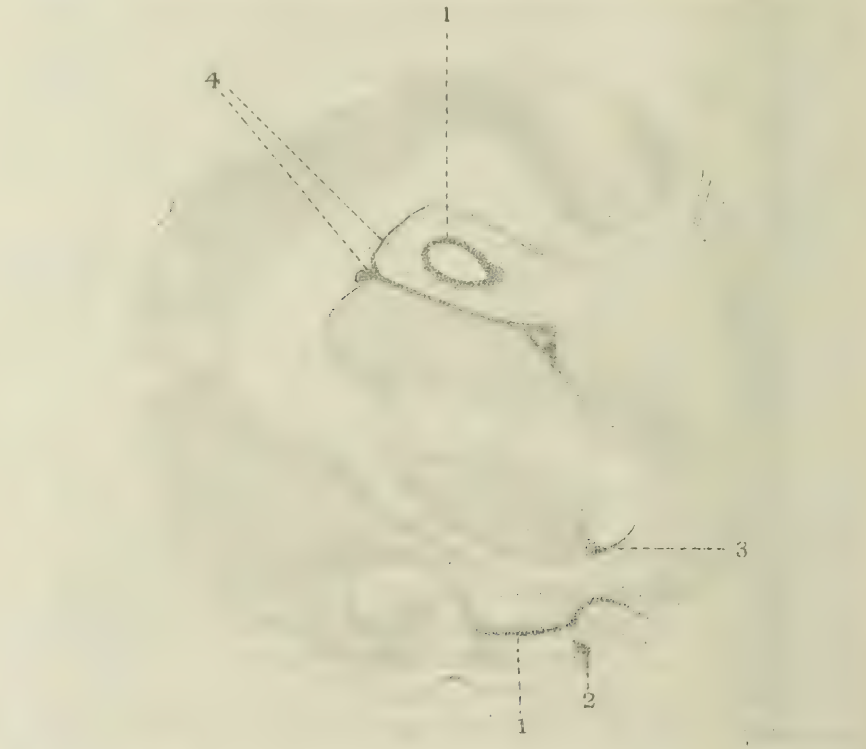


FIG. 1.—Celloidin section stained with thionin. (Zeiss, Oc. 0, Obj. a, 2.) (1) A layer of pyramidal cells in the cornu Ammonis. (2) An inflammatory focus. (3) An inflammatory focus in the lenticular nucleus. (4) Inflammatory infiltration of ependyma and choroid plexus of the lateral ventricle.

Pathological Changes.

The pathological changes are identical in both infections. Although there are three forms of the disease, acute, subacute and chronic, the changes in the brain may be described as either acute or chronic.

Pathological Changes in the Acute Form.

Rabbit No. 25 was inoculated subdurally with a brain emulsion of a patient dead of encephalitis lethargica. Macroscopically the brain showed some slight congestion. Microscopically there was a well marked infiltration of the pia mater all over the brain, most marked at the base and in the neighbourhood of the optic and oculo-motor nerves, and from here the inflammation penetrated into the brain tissue. The pia mater over the cerebellum was only slightly infiltrated. In some places the blood-vessels showed perivascular infiltration, chiefly in the superficial layers of the base. In the brain tissue, and principally in the region of the lenticular and caudate nuclei, there were foci of cellular infiltration which was most marked on the ventricular side of the caudate nucleus (fig. 1). No inflammation was found in the cerebellum, pons or medulla oblongata. The infiltration consisted of mononuclear elements, large mononuclear cells and lymphocytes (fig 2). Degenerative changes, in the form of chromatolysis, were present throughout the nervous system; it was less marked in the cortical cells than in those of the caudate and lenticular nuclei. The Purkinje cells in the cerebellum had undergone marked chromatolysis; some of them had disappeared completely and were replaced by neuroglia, or only traces of them remained. The small cells of the zona molecularis

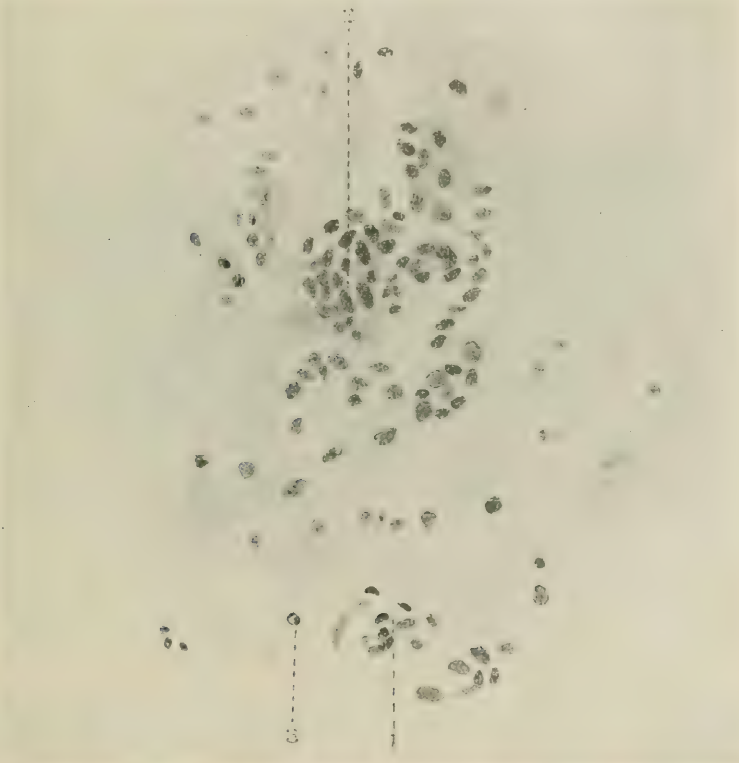


FIG. 2.—Inflammatory focus in the lenticular nucleus. (Zeiss, Oc. 2, Obj. DD.) (1) A large mononuclear cell. (2) A group of large mononuclear cells. (3) A lymphocyte.

showed the degenerative changes described by Simchowitch; the nucleus was contracted, the chromatin granules arranged on its periphery, the protoplasm dissolved gradually and finally surrounded the nucleus as a small zone, separated from it by a lighter one. In the last stages of degeneration the cells come to resemble plasma cells. We found similar changes in the locus niger of Soemmering, and marked chromatolysis in the cells of Deiters' nuclei and in the dentate nuclei of the cerebellum.

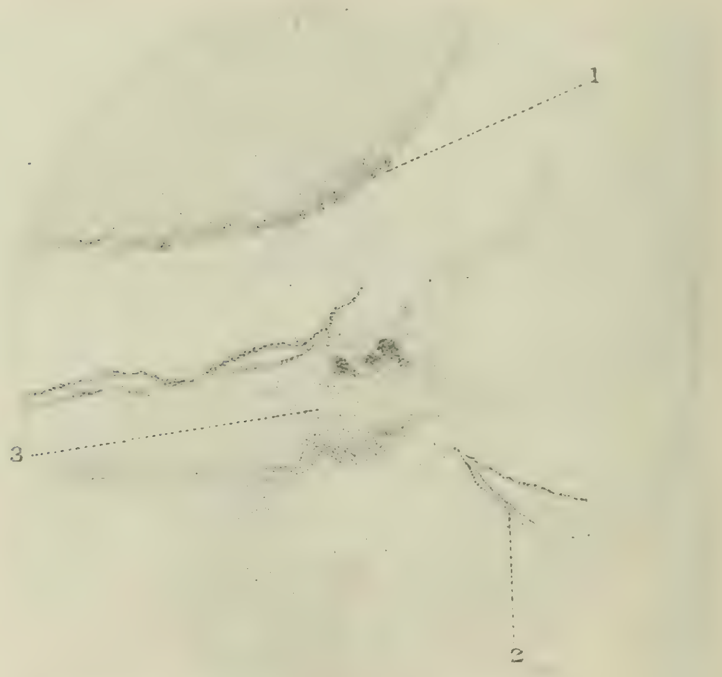


FIG. 3.—(Zeiss, Oc. 0, Obj. aa). (1) Cortex. (2) A patch of inflammatory infiltration. (3) An inflammatory focus between the optic thalamus and the cortex.

The disease ran a more acute course in a rabbit inoculated on April 1 subdurally and into the right eye with a brain emulsion from another rabbit infected with encephalitis lethargica. It died eight days later without showing any clinical symptoms. In the pia mater over the base of the brain, and in a lesser degree in the choroid plexus of the third ventricle, there was a cellular infiltration. The blood-vessels were only slightly infiltrated and the pia mater was hardly infiltrated at all except over the fissure separating the cerebellum from the medulla oblongata where we found marked infiltration round the blood-vessels. Inflammatory changes were on the whole slight, but the degenerative lesions were very striking. There was marked chromatolysis of the cells of the optic thalamus, in those of the nuclei of the floor of the fourth ventricle and even in the anterior horns of the cord. Some cells had disappeared completely. The zona molecularis of the cerebellum showed the same changes as in rabbit No. 25. In the cells of Deiters' nuclei the Nissl's corpuscles were completely disintegrated, the nucleus was swollen and situated excentrically, in places the protoplasm did not stain at all, and of some cells only traces remained.

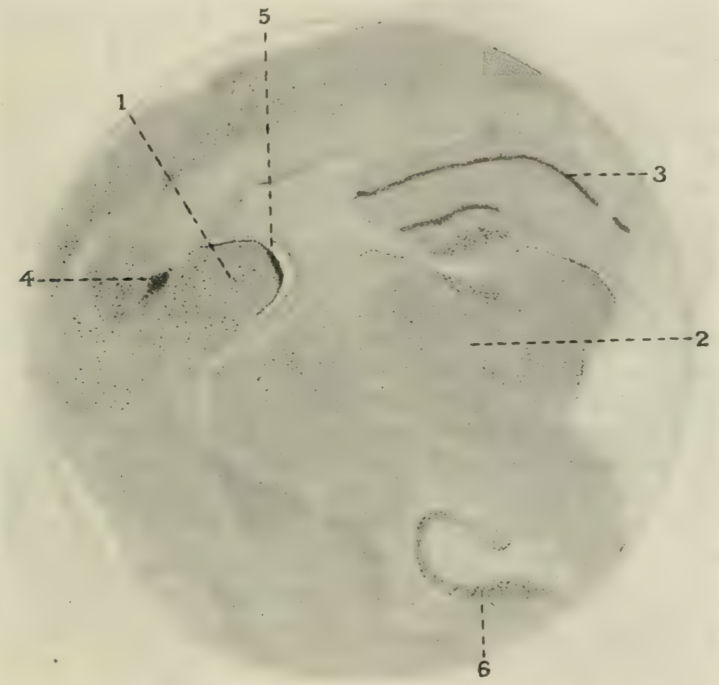


FIG. 4.—(Zeiss, Oc. 0, Obj. a2). (1) Nucleus caudatus. (2) Optic thalamus. (3) A layer of pyramidal cells in the cornu Ammonis. (4) An inflammatory focus. (5) The lateral ventricle. (6) The cornu Ammonis.

These pathological changes were typical. The mononuclear infiltration was a constant feature, even in the most acute cases that proved fatal within two days.

Rabbit No. 6: Small size, albino. Inoculated on March 11 under the dura mater with brain emulsion from rabbit No. 2, died March 13. In spite of the short duration there were typical changes in the usual regions: in the base of the brain, in the periphery of the nucleus caudatus, in the wall of the lateral ventricle and in the region of stratum zonale of the optic thalamus. The infiltration consisted of mononuclear elements, except at the base of the brain where a few polynuclear cells were found. We may say that the mononuclear infiltration was typical for both infections. Our observations differ in this from Levaditi and Harvier, who found mononuclear infiltration in the chronic forms and polynuclear cells in the acute cases. Our observations seem to confirm the views of Bergel who states that some bacteria of a lipoid nature, as Koch's bacillus, cause a mononucleocytosis.

We have described rabbit No. 21a as an example of a subacute infection (p. 57).

Examining its brain we found in the pia mater over the base of the brain a marked infiltration which penetrated into the brain tissue for a few millimetres. There were small foci of cellular infiltration scattered about, most numerous in the caudate and lenticular nuclei. The walls of the blood-vessels were thickened, the adventitia had proliferated, and the lumen of the vessels was in some places completely occluded. There was marked perivascular infiltration ("manchons perivasculaires"), especially in the above mentioned nuclei. Between the vessels the tissues were infiltrated with mononuclear cells, plasma cells and elongated cells resembling Stäbchenzellen, and by granules resulting from destruction of the cells. There was marked proliferation of neuroglia. No inflammatory changes were found in the cerebellum. A few neurophages were seen in the cortical cells. The degenerative changes were similar to those described above; they were most marked in the Purkinje cells and in Deiters' nuclei and least evident in the cortical cells. The ocular muscles were also infiltrated.

Consequently the only difference between the last observation and the two others was the presence of neurophages and plasma cells, and the thickening of the walls of the vessels.

Pathological Changes in the Chronic Form.

Inflammatory changes.—We may mention as an example rabbit No. 1 which had been inoculated into the eye with the contents of a herpetic vesicle.

The inflammatory changes were discrete. There was a slight infiltration of the pia mater over the base and convexity of the brain, seen clearly in a transverse section through its anterior part. A few inflammatory cells were also found in the ependyma of the lateral ventricles. There were scattered inflammatory foci in the caudate and lenticular nuclei and in the septum pellucidum. In a more posterior transverse section (figs. 2 and 5) a large inflammatory focus was seen in the angle between the caudate nucleus and the cortex, and a smaller one in the nucleus amygdalæ. There was a hæmorrhage and some infiltration on the surface of the thalamus and in the pia mater over the cerebral peduncles: the locus niger of Soemmering contained small inflammatory foci and there was some infiltration of the blood-vessels in the caudate and lenticular nuclei. The infiltration consisted of mononuclear elements (lymphocytes and here and there plasma cells). (Fig. 6.)

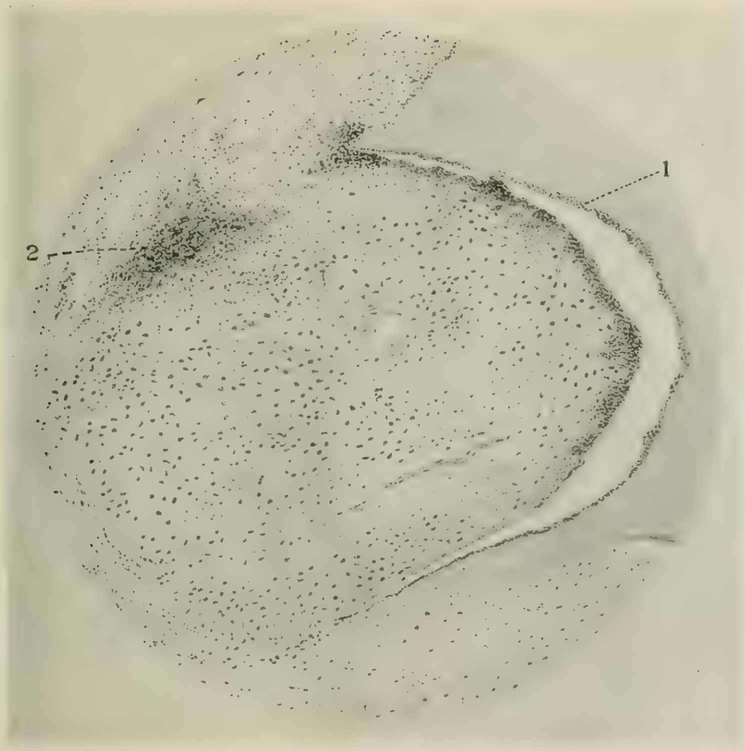


FIG. 5.—An inflammatory focus in the caudate nucleus. (Zeiss, Oc. 2, Obj. aa.) (1) Ependyma of the lateral ventricle. (2) An inflammatory focus.

Degenerative changes.—Degenerative changes were very marked in the nerve cells. In the cortical cells we found chromatolysis and vacuoles; the Purkinje cells had partially disappeared; those of the red nuclei stained with difficulty, their nuclei were swollen and they were surrounded by neurophages; the cells of the third nerve nuclei had also undergone chromatolysis.

From this description we see that in the chronic cases there is much less small cell infiltration than in the acute cases, but more proliferation of the connective tissue in the meninges, and in the nervous tissues polyblasts and plasma cells are found. Degenerative changes, on the other hand, were prominent in all of them. In a few rabbits, however, in which the disease ran an acute course, post-mortem examination revealed the same predominance of degenerative changes.

Rabbit No. 20, albino, 440 grm. weight. Inoculated into the right eye with a brain emulsion of rabbit dead of encephalitis lethargica. It died on the eighth day. There was very slight infiltration in the region of the optic nerves and in the medulla oblongata an inflammatory focus, consisting of mononuclear elements surrounded by neuroglia, was present. The degenerative changes were marked and not of the usual type; in the cells of the caudate nucleus and of the cornu Ammonis the protoplasm stained with difficulty, and in some cells only the nuclei, which were large and stained poorly, contained a large spindle-shaped nucleolus with dark well-stained corpuscles at both ends; this appearance suggested a mitosis (fig. 7). In some nuclei there were two such structures, but other nuclei contained several

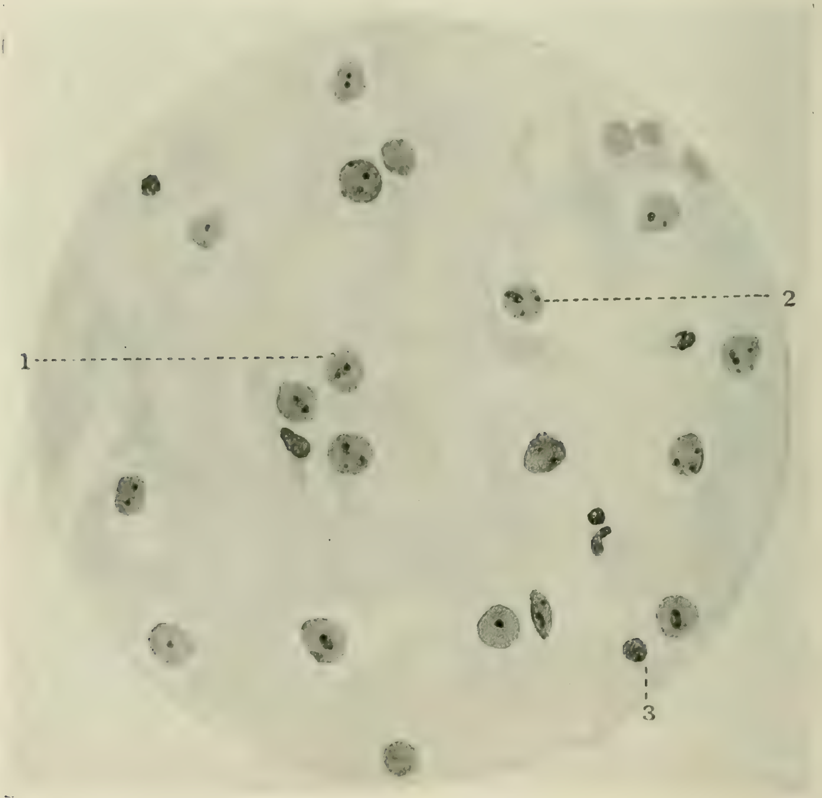


FIG. 6.—The inflammatory focus seen in fig. 5. (Zeiss, Oc. 2, Obj. immersion.) (1) A large mononuclear cell. (2) A lymphocyte.

small corpuscles in addition to the nucleolus. The cells of Purkinje and those of the grey matter in the floor of the fourth ventricle showed beginning chromatolysis.

The brains of rabbits which died without developing clinical symptoms presented post-inflammatory scarring of long standing; such changes were found in all animals killed some time after infection.

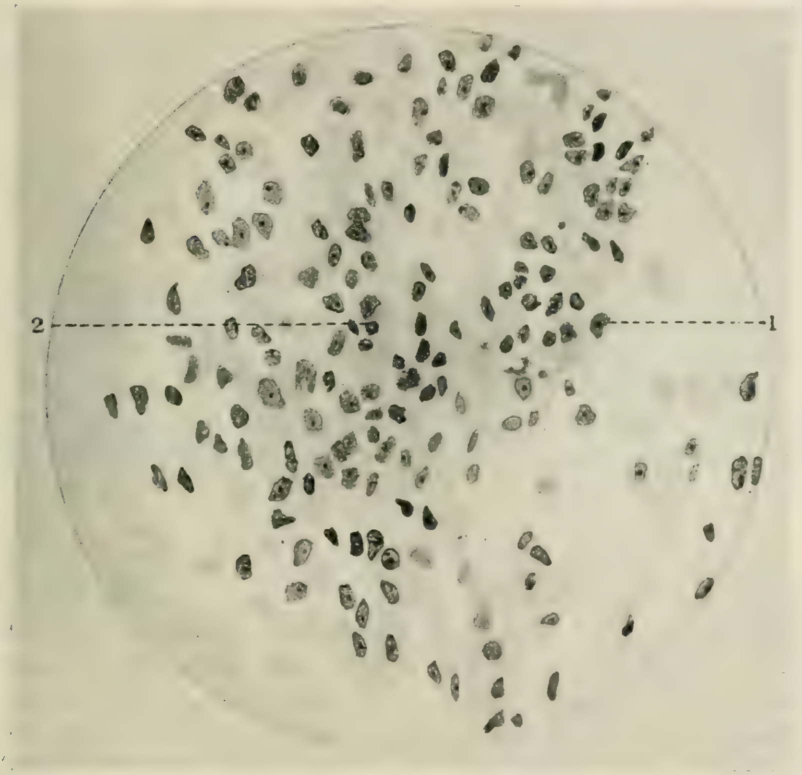


FIG. 7.—The caudate nucleus. (Zeiss, Oc. 2, Obj. immersion.) (1) A nucleus of a nerve cell with its spindle-shaped nucleolus. (2) A nucleus with a spindle-shaped nucleolus and two corpuscles. (3) A neuroglia cell.

Oliver, however, found in 20 per cent. of normal rabbits inflammatory changes of long standing, indicating some previous inflammation of the brain.

The rabbit No. 31 helped to determine the origin of the labyrinthine symptoms so often met in our investigations.

Old post-inflammatory changes were found at the base of the brain, the pia mater being thickened and containing a great amount of fibroblasts and connective tissue; the intima and adventitia of the blood-vessels were proliferated, and here and there in the cortex and thalami there was a mononuclear infiltration of their walls. In one place, on the border of the pia mater and cortex, there were traces of an old inflammatory focus, consisting of fibroblasts, plasma cells and polyblasts. In transverse sections more posteriorly a more intense infiltration of the pia mater over the base was found, especially at the level of the corpora quadrigemina. No inflammatory changes were discovered in the brain tissue, except in the nucleus of the nervus vestibularis and in the tuberculum acusticum. The cells of the nucleus vestibularis were degenerated. Slight changes were also found in the cells of Deiters' nuclei and of the nuclei of the floor of the fourth ventricle, but the cells of the cerebellum, red nuclei and nuclei dentate were not affected.

In this case the inflammatory changes were slight except in the nucleus vestibularis; this explains the circus movements of the animals.

We are at present unable to say why animals so often develop these circus movements and disturbances of static position which are never met in man. It may be that in animals the virus has a selective affinity for the nervus vestibularis as it has for the oculomotor nuclei in man, or it may be due to a special arrangement of the blood-vessels or to some biochemical properties of these nuclei.

Changes in the Liver.

In all our animals infected with either virus we found inflammatory changes in the liver. These consisted of a mononuclear infiltration round the small bile ducts, the inflammatory cells often penetrating between their epithelial cells which were occasionally much proproliferated. The liver was congested and the cells around the blood-vessels were often destroyed. Such changes were not found in the spleen and kidneys. The relation between affections of the grey matter of the brain and diseases of the liver were first pointed out by Wilson, who found that affections of the lenticular nucleus were often accompanied by cirrhosis of the liver. Wilson considered the liver affection as primary, the brain being secondarily affected as result of disturbed metabolism. Our experiments suggest that both organs were affected simultaneously. The livers of patients who have died of encephalitis lethargica contain changes similar to those we found in the rabbits, but as we have not yet been able to examine many human livers, we cannot come to definite conclusions.

Our experimental work on the liver has been only recently undertaken. We have proved, however, that the infiltration of the bile ducts is not merely due to toxins or to disturbance of metabolism, since by injecting animals with an emulsion of liver tissue in the same way as we did with a brain emulsion, we have been able to reproduce the disease, and therefore to show that the virus itself is localized in the liver.

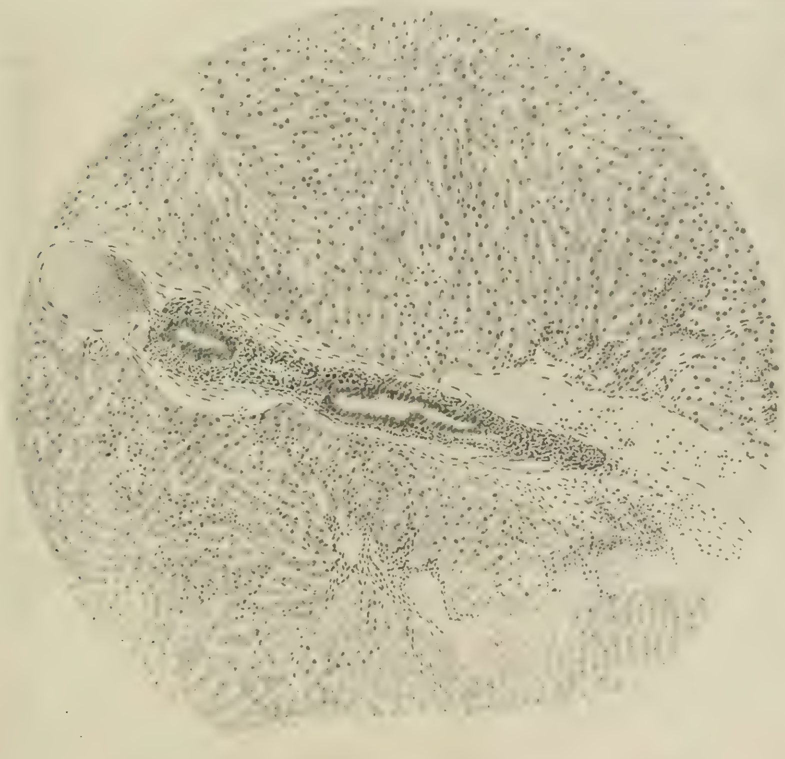


FIG. 8.—(Zeiss, Oc. 2, Obj. aa.) Infiltration of the bile ducts in the liver.

There are many characters common to the infection of man and animals; the infiltration consists of mononuclear cells in both, its localization in the basal ganglia was also similar, and degenerative changes in the cerebellum occur in man as well as in the rabbit. We have been able several times to demonstrate marked degenerative changes in the Purkinje cells in man, though inflammatory changes were absent. The meninges, however, react differently, since in man their affection plays an important part in the pathological picture. This seems to contradict Levaditi s view of the ectodermotropic nature of the virus, that is to say, its special affinity for the tissues of ectodermal origin. That the liver is also involved is another argument against his hypothesis.

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DYSTROPHIA MYOTONICA (MYOTONIA ATROPHICA).

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I.—Introduction.
II.—Description of Cases.
III.—General Description of the Disease.
    (1) Onset and course.
    (2) Myotonia and muscular atrophy.
    (3) Cataract.
    (4) Other extra-muscular symptoms.
IV.—Heredo-familial Features.
V.—Pathology.
VI.—Conclusions.

I.—Introduction.

The history of the disease we are about to consider may be said to begin in 1886 with the appearance of Erb's monograph on Thomsen's disease; for although myotonia congenita and myotonia atrophica are distinct conditions, Erb's work, by arousing widespread interest in myotonia in general, led to the publication of a large number of cases of so-called atypical Thomsen's disease and this brought to light the group of cases that now concerns us in which myotonia is associated with atrophy of the muscles.

This curious combination of symptoms was described for the first time by Deleage in 1890; thereafter isolated cases were recorded by Hoffmann, Jolly, Kornhold, Nogues and Sirol, Schultze, Berg, Curschmann, Fürnrohr and others, but no real advance was made until 1909, when Batten and Gibb [4] and Steinert [54] gave independent descriptions of the clinical features of this group and showed that it constituted a distinct and characteristic symptom-complex. Unlike earlier writers, who detected no uniformity in the distribution of the atrophy, these observers found that it was constant in certain positions, namely in the face, where it gave rise to the facies myopathica, in the muscles of mastication, the sternomastoids, the forearms, and, less often, in the peronei; but whilst they agreed on many points they differed in their conception of the nature of their cases and the sequence of the symptoms, for Steinert maintained that myotonia was the essential and initial symptom, atrophy being merely an incident in the course of Thomsen's disease, whereas Batten gave priority to atrophy, and, holding that myotonia was "merely a symptom," placed his cases in a group amongst the myopathies.

Time has confirmed the general accuracy of their descriptions of the muscular symptoms; but it has also brought into prominence a number of extra-muscular phenomena, some of which, though noticed before, had been regarded as fortuitous, and has brought about a complete change in our conception of the nature of a disease, which, far from being an affection of the muscular system alone, is now known to be a general dystrophic disorder with diverse and widespread manifestations.

This significant change followed closely upon the discovery that cataract was a frequent symptom. In 1911 one of us [16] described a family of thirteen brothers and sisters, of whom five suffered from myotonia atrophica, two with and three without cataract, and two from cataract alone. In the same year accounts of patients with myotonia atrophica and cataract were published by Kennedy and Oberndorf [34] and Ormond [44] and thereafter the number of similar observations increased rapidly. At once the other extra-muscular symptoms, as atrophy of the testicles, baldness, loss of body weight, and the rest, which had hitherto been regarded as more or less accidental, were viewed in a new light. In 1912, Curschmann [8], who was the first to recognize their significance, elevated them to a cardinal position at least equal in importance with myotonia and muscular atrophy in the symptomatology of the disease, and insisted that they must receive full consideration in any discussion on its nature. At the same time he expressed his agreement with Lewandowsky [37], Hirschfeld [27] and Grund [19], who had already in separate papers declared the independence of these cases from Thomsen's disease, and gave his classical description, to which little of material importance has since been added. According to this description the main features of the disease are briefly: Onset between the ages of 20 and 30 years in contrast to the earlier onset of Thomsen's disease; muscular atrophy of peculiar distribution as described by Batten and Steinert, namely facies myopathica with atrophy of the sternomastoids and the muscles of the forearms; myotonia confined to a few muscles and usually present in the hand-grasps alone; loss of tendon reflexes; extra-muscular symptoms, of which the most frequent are cataract, baldness, atrophy of the testicles and impotence ; various vasomotor disturbances, and general atrophy and loss of weight.

At this stage in its history dystrophia myotonica was regarded as a distinct disease characterized by the triad, muscular atrophy of peculiar distribution, myotonia and certain extra-muscular "dystrophic" symptoms.

In recent years, however, its status has changed again, for Fleischer's [12] investigations into the family history of patients presenting this combination of symptoms have shown that this syndrome is but one aspect of an heredo-familial disease whose presence may be expressed in divers ways.

The changes that have occurred in the status of the disease from time to time are reflected in the names it has borne. The early designation, "Thomsen's disease with muscular atrophy," is a reminder of a period when myotonia and Thomsen's disease were synonymous and when any patient with myotonia, though deviating in any respect from Erb's classical description, was described as an atypical case of Thomsen's disease. In 1901 Rossolimo [48] proposed the name "myotonia atrophica" for those cases in which atrophy was supposed to have supervened in the course of Thomsen's disease, and this name has been retained in this country, although the two diseases are now known to be separate. In recent years the name proposed by Curschmann—dystrophia myotonica—has been adopted, because it emphasizes the dystrophic phenomena; but it is certain that finality in nomenclature has not been reached, because a name is still required which will designate the heredo-familial disease of which the syndrome dystrophia myotonica is a part. The name proposed by Naegeli [41]—"pluriglanduläre Erkrankung innersekretorischer Drüsen"—and the ideas it connotes are not likely to prove acceptable at present, for although it is clear that the underlying defect is an endogenous one, the evidence available does not support Naegeli's contention that the primary defect is in the ductless glands.

Since 1912, when Curschmann gave his classical description of dystrophia myotonica, much has been written upon the subject and the number of the recorded cases already approaches two hundred ; nevertheless, the time has not yet arrived when descriptions of new cases are devoid of interest, for our information is still incomplete on many points, and a number of problems remain for the solution of which reports of careful investigations on a large number of cases are still necessary. Further, very few cases have been examined after death, and our knowledge of the morbid anatomy of the disease is still meagre. We are able to give here an account of the findings in a case which was the first, so far as we are aware, to come to autopsy in this country; and descriptions are given of the morbid appearances in portions of muscle removed from two patients during life. In our general description of the disease we base our remarks upon twenty cases that have come under our own observation, and at the same time we draw freely upon a large number of papers that have appeared in foreign journals since this disease last formed the subject of a communication to English readers.

II.—Description of Cases.

Case 1.—William A., an army pensioner, aged 44 years, was admitted to the National Hospital under the care of one of us in February, 1922, complaining of "weakness in the arms and legs" of five years duration. He enjoyed good health until March, 1917, when, whilst undergoing military training, he underwent a severe feverish illness diagnosed as influenza. During convalescence from this illness he suffered from severe pains in the joints, especially in the knees, elbows and shoulders; the pains disappeared in a few months but left behind them a weakness in the legs, which soon spread to the arms and increased gradually as time went on. Early in 1918 he noticed for the first time an occasional difficulty in relaxing his grasp; the more firmly he grasped an object the more difficult it was to relax his hold. This symptom still troubles him. He cannot say with certainty whether this difficulty preceded or followed the onset of weakness in the arms, but he thinks that weakness came first. During the last year he has noticed a feeling of stiffness in the legs on rising to his feet and slowness in "getting off the mark" when he begins to walk: after the initial stiffness has worn off he can walk at a slow pace for about a quarter of an hour; the legs then begin to ache and he is forced to rest. He is quite steady on his feet, but on several occasions the legs have given way suddenly without apparent cause and he has fallen "like a log" in such a way that he has struck the back of his head. His weight is two stone less than it was before his illness began; his arms and legs have wasted and his facial appearance has altered very much during the last few years; his voice is not so clear as it used to be; his hair has fallen out freely, especially in front of his head; he has had no sexual intercourse for several years and desire is absent; his hands are "naturally cold" and they often "go blue"; his eyes water freely, especially when he is in the open air. Apart from weakness of the limbs he feels perfectly well. His eyesight is very good; he has no difficulty in chewing his food or in swallowing; the amount of sputum is not increased and he hardly ever perspires.

He was always very healthy until his present trouble began; he played football in his youth and was an unusually good long distance walker. For ten years before joining the Army he did heavy manual work in a mineral-water factory.

His parents died when he was a child from causes unknown to him; he has three sisters, all older than himself and all healthy; his only brother died in childhood of pneumonia. He has three daughters and one son living; one son died in infancy of pneumonia.

So far as he knows no member of any branch of his family has suffered from any muscular trouble or from cataract. One of his sisters and his only son were examined by us and found to be healthy. The son is a professional long-distance walker of repute; on one occasion he walked from his home to visit his father in hospital and returning on foot covered a distance of over one hundred miles in twenty-three hours.

Condition on examination: Height, 5 ft. 6 in.; weight, 7 st. 4 lb. Skull of normal size and shape; ears small, well-formed; face lacks expression, deep temporal hollows, sunken cheeks, smooth forehead, drooping eyelids, rather thick, slightly pursed lips. Skin on forehead very greasy, giving it the appearance of being covered with sweat; conjunctivæ slightly injected, eyes watery; tongue small and deeply furrowed; palatal arch very high and narrow; many teeth missing, many stumps, no prognathism; hair black, thin on vertex, marked frontal baldness; thin dark eyebrows, strong dark beard, shaves daily. Thyroid gland neither visible nor palpable; chest hairless, axillary and pubic hair scanty; nipples deeply pigmented; pubic hair of normal male distribution; no hair on arms or legs. Penis well formed and of normal size, testicles small and very soft; hands cold and blue, nails brittle, with deep longitudinal ridges, no lunulæ visible; texture of the skin normal, very little subcutaneous fat. Heart apex in fifth space in nipple line, sounds feeble, no murmurs; pulse regular, vessels healthy, average rate 80 per minute: blood pressure (Riva Rocci), systolic 105, diastolic 70 mm. Hg: lungs healthy.

Electrocardiogram (Dr. E. D. Adrian): "It has been stated that there is sometimes a lengthening of the A-V interval in patients with this disease. We therefore recorded the electrocardiogram leading from the right hand to the left foot. The A-V interval, or rather the P-R interval (between the summits of the P and R waves) was 0·16-0·17 second over a large number of cycles. This is well within the limits of the normal."

Barium meal (Dr. Russell Reynolds). Form and motility of stomach normal; no delay in passage through intestinal canal.

Urine: Specific gravity 1,015; contained no albumin or sugar. Blood count: Red blood cells 4,700,000, hæmoglobin 92 per cent; white blood cells 7,000, polymorphonuclear cells 65 per cent., lymphocytes 33 per cent., eosinophils 2 per cent.

Nervous and muscular systems.—The patient is even-tempered and sociable and submits with good grace to prolonged examinations; memory very good, takes an intelligent interest in his disease and is well-informed. His expressionless face gives an impression of dulness and mental apathy which further acquaintance with him soon belies. Speech low-toned, monotonous and slightly muffled. Vision $\frac{6}{6}$ in both eyes; "no cataract, fundus normal" (Mr. Leslie Paton). Hearing, smell and taste normal. Pupils of moderate size, equal, and regular in outline, react well to light and on convergence; range of ocular movements complete, no nystagmus; corneal reflexes brisk and equal; temporal muscles wasted, masseters small but firm, and their power is slightly diminished. Typical myopathic facies with weakness of all the facial muscles, most marked in the orbiculares oculi; well-marked Chvostek's sign on both sides. Soft palate is not unduly thin, moves well on phonation, palatal reflex present, no dysphagia. All movements of the vocal cords appear to be normal on inspiration and phonation, although the appearance of the right cord leads one to infer that it is less tense than the left. The condition, however, is not sufficiently marked to be acceptable as evidence of definite paresis. The tongue is small and deeply wrinkled, and can be protruded with difficulty about half an inch beyond the teeth; on striking its lateral border with a small percussion hammer a deep dimple forms and persists for several seconds.

The neck is thin, the box of the larynx is unduly prominent, all the muscles of the neck are weak and wasted; deep hollows replace the normal prominence of the sternomastoids which are represented by a few fibrous strands; in the erect position the head is held bent forward; when he is lying down the head cannot be raised from the pillow, and when the trunk is raised the head falls back; the upper parts of both trapezii are slightly wasted, but the shoulders can be shrugged powerfully. There is no atrophy of any of the muscles of the shoulder-girdle, and the range of voluntary movement at the shoulder-joint is complete, though there is definite slight loss of power in all movements; no wasting in the upper arms, range of movement at the elbow complete, power of flexion very good, extension not quite so good; obvious wasting of all the muscles of the forearms, greatest in the extensors, especially in the supinator longus; extension at the wrist very feeble, flexion weak but better than extension; hand-grasps feeble; dynamometer R.30, L.28 (observer R.120, L.118); slight wasting of the muscles of the thenar and hypothenar eminences and power diminished out of proportion to the wasting; cannot touch tip of little finger with tip of thumb; writes rapidly with a pen in a good hand. No wasting of trunk muscles, but he is unable to rise from the supine to the sitting position without using his arms; repeated flexion and extension of the spine in the standing position is carried out slowly and soon tires; the muscles of the buttock are small and soft but not obviously wasted; power of all movements at the hip-joints is greatly diminished; when lying on his back the extended lower limb can be raised about 45°, but the attitude cannot be maintained for more than a few seconds. Flexion and extension at the knee-joint are weak, flexion being better than extension. The muscles on the antero-lateral aspect of the leg are definitely wasted; the calves are soft but bulky in comparison with the other muscles of the lower limbs; dorsiflexion of the feet is very weak, plantar flexion less so; throughout the lower limbs the loss of power is much greater than the amount of wasting would suggest. The muscles generally are small and soft, the limbs are limp and offer little resistance to passive handling; all voluntary movements are well co-ordinated when he carries them out at his own slow pace, but alternating movements, especially when he attempts to perform them rapidly, are badly done; in attempting rapid alternating flexion and extension at the elbow for example, after the action has been repeated once or twice extension is begun before flexion is complete and vice versa, and later he begins to make adventitious movements at the wrist and shoulder-joints, so that after a time the arms are flung about in a most disorderly manner, the desired movement of flexion and extension being almost absent. The same defects of voluntary movement are present in the lower limbs; their explanation will be discussed later in the chapter on myotonia. All the tendon reflexes are absent.

The patient stands on a wide base with the head bent forward; there is a marked upper dorsal kyphosis and compensatory lumbar lordosis; he walks slowly with a slight "steppage" gait; in attempting to rise from the floor he proceeds in exactly the same manner as a patient with pseudo-hypertrophic paralysis up to the point of assuming the all-fours position, but he is unable to climb up his legs and is quite unable to gain the erect position; he cannot rise from a chair without using his arms. Fibrillation was observed in the thigh muscles on several occasions.

Myotonic symptoms: Myotonia on voluntary movement is extreme in the hand-grasps; on grasping the observer's hand firmly an associated movement of flexion occurs at the wrist; when the order is given to relax, the grip loosens at once and the fingers are extended just enough to allow the hand to be withdrawn; the fingers remain flexed at the metacarpophalangeal joint for many seconds, and flexion of the wrist persists for thirty seconds or even more; the difficulty in extending the fingers and wrist is greater the more power he exerts; it diminishes and then disappears with repetition of the movement. A similar delay in relaxation was demonstrable in the biceps and deltoid of both sides and in the extensors of the knees.

On stimulating the muscles mechanically by a firm blow with a percussion hammer a prolonged contraction, lasting sometimes as long as thirty seconds, was obtained in the tongue, the deltoids, the thenar and hypothenar eminences, the vastus externus and the calves. In the tongue the phenomenon is shown by the formation of a deep dimple on the lateral border at the point of impact; in the deltoids, where the prolonged contractions are most persistent and most easily elicited, a deep hollow forms at and around the point of impact: it is broadest at this point and is continued up and down in the length of the fibres as a distinct furrow; this is seen in the vasti and calves as well. In the thenar eminence the muscles stand up prominently and the thumb is strongly adducted; in the hypothenar eminence the muscle stands out, the little finger is abducted and remains in this position for ten seconds or more. It is noticed that in the muscles showing much atrophy the normal myotatic irritability is absent, and that the myotonic after-contraction is most easily demonstrated in the muscles that have retained their bulk. In the pectoral muscles, however, sharp percussion produces a typical "harp-string contraction" of normal duration, whilst at the point of impact a little elevation forms and persists for a few seconds, just as it does in many healthy individuals.

Electrical reactions.—To direct faradism the excitability of the following muscles was greatly diminished: Flexors and extensors of the forearm, extensors of the knee and dorsiflexors of the foot. No response was obtained from the sternomastoids or from the tibialis anticus. Normal twitches were obtained from all the other accessible muscles: in the deltoids, the flexors of the forearm and the soleus of both sides, short stimuli evoked a normal twitch; with a stimulus of longer duration the contraction persisted as long as the current was passing and for several seconds after it was withdrawn.

To direct galvanism no reaction was obtained from the sterno-mastoids or tibialis anticus, and the excitability of the extensors of the forearms, extensors of the knees and the dorsiflexors of the feet was greatly reduced; in several muscles A.C.C. was definitely greater than K.C.C. From a number of muscles—e.g., deltoids, thenar and hypothenar eminences, extensors of knee, hamstrings, solei and peronei—normal twitches could not be obtained, but a tetanic contraction occurred and persisted as long as the current was passing; as a rule the muscle relaxed as soon as the stimulus ceased, but in the deltoids, small muscles of the hands and solei, there was a myotonic after-contraction; this phenomenon was evoked more readily from the anode than from the cathode.

Dr. E. D. Adrian kindly undertook the investigation of the electrical reactions of the muscles and has given us the following report:—

The response to electrical stimulation.—The curve relating the strength and duration of current required to excite [1] was determined for two muscles, the deltoid and the flexor carpi radialis of the right arm. Both these muscles gave well-marked myotonic phenomena, but the strength-duration curve shows nothing abnormal. This may be seen from fig. 1 which gives the curve for the flexor carpi radialis and, for comparison, a curve for the same muscle in a perfectly healthy subject. The chronaxie (the duration corresponding to a strength twice as great as the threshold value at infinite duration) is 0·0002 second for the flexor carpi radialis and 0·00015 second for the deltoid, the range of variation in healthy subjects being 0·00008 second to 0·0006 second. The absence of any marked change in the curve is not to be wondered at in view of the fact that currents of short duration probably take effect on the motor nerve fibres and not on the muscle substance itself.

With currents of long duration the response was abnormal. (1) For example, with the galvanic current when the key was opened and closed by hand the muscle remained contracted as long as the current was passing instead of contracting at make and break only. We are unable to say whether this persistent contraction was localized to the neighbourhood of the electrodes, but it did not cause any marked shortening of the muscle. (2) With very strong currents (over ten times the threshold value), even though the duration was shorter than 0·001 second, the muscle relaxed slowly. (3) With intermediate durations (0·05 second), even with weak current strengths a double twitch of the muscle was often observed. (4) With weak currents of less than 0·001 second duration, such as single shocks from a faradic coil, the muscle twitch showed no departure from the normal. Myographic tracings of such muscle twitches gave a rapid rise and fall exactly like that of a normal muscle.

These results point to an abnormality in the muscle fibre rather than in the nerve, but they do not allow us to go any farther in suggesting the nature of the abnormality.

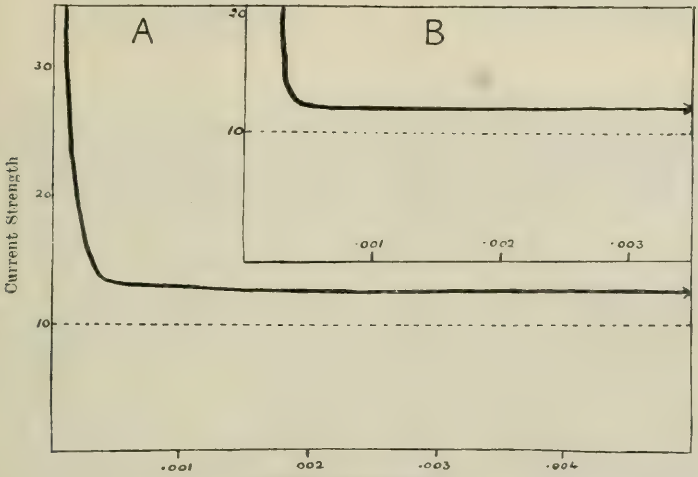
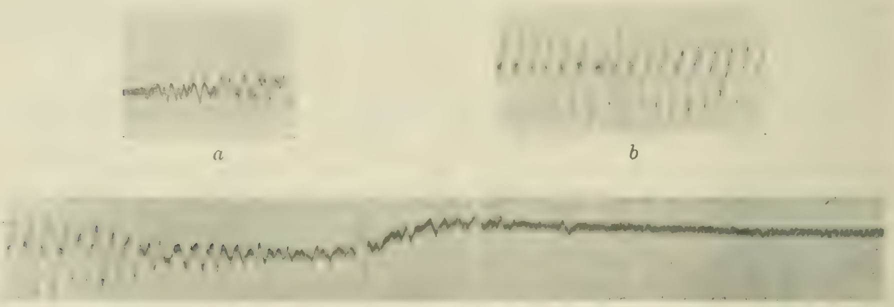


FIG. 1.—*Case* 1. "Chronaxie" curves for (A) flexor carpi radialis in Case 1, and (B) for normal muscle.

The electromyogram.—The action current in the deltoid during voluntary contraction was recorded with the string galvanometer. Non-polarizable electrodes (Zn, ZnCl, NaCl) were strapped to the shoulder and the patient was made to contract the muscle against resistance. A typical record is shown in fig. 2. This gives the irregular action currents at the beginning of the contraction (fig. 2, *a*), and the more regular oscillations occurring after the contraction had been maintained for two and a half seconds (fig. 2, *b*). A very irregular rhythm at the beginning of a contraction and a more regular one later on is not very uncommon in a normal muscle, though the regularity in this case seems to be greater than usual. The oscillations have the normal frequency of about fifty a second.

The most interesting part of these records occurred when the patient was told to stop contracting. The large oscillations cease in about half a second, and after this the string shows no more than the usual very small irregularities which are present when the muscle is at rest (fig. 2, *c*). The muscle does not relax completely, however, until ten to fifteen seconds after the order to stop. Thus the persistent after-contraction is not accompanied by an oscillating electric response of the type found in the voluntary contraction; in fact it is not accompanied by any electric response that could be detected by the means at our disposal. (It should be mentioned that we were not working with a specially sensitive system.)



a *b*

c

FIG. 2 (*a*, *b* and *c*).—*Case* 1. Tracings taken by string galvanometer of the voluntary contraction of the deltoid muscle in Case 1 (*a*) at the beginning of contraction; (*b*) during contraction; (*c*) during relaxation. At the beginning of the tracing (*c*) the patient was told to relax the muscle, which, however, remained in contraction for about ten seconds longer, although the nervous stimuli to it, as shown by the galvanometer tracing, ceased in less than one second. The waves of nervous impulse are at a rate of about fifty per second.

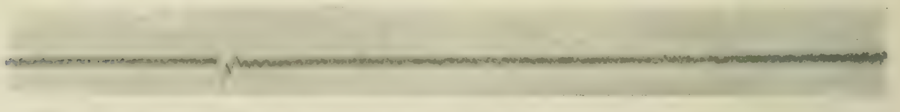


FIG. 3.—*Case* 1. String galvanometer tracing, showing the effect of direct percussion of the deltoid muscle. A single wave is shown by the galvanometer, although the contraction of the muscle persisted for several seconds.

The same holds good for the persistent local contraction produced by striking the muscle with a percussion hammer (fig. 3). The blow itself caused a rapid displacement of the string, which may have been due to a shifting of the electrodes or may have been a single action current, but the string returned to rest long before the local contraction had subsided.

The absence of electric response in the myotonic effect can be most simply explained on the following lines. There can be little doubt that the large electric oscillations are due to impulses of nervous origin sweeping through the muscle. These cease when the patient stops contracting voluntarily. The persistent after-effect in the myotonic muscle is therefore not maintained by impulses from the central nervous system, but is due to some abnormality in the muscle fibre. A persistent contraction of this type need not be associated with any form of electric response, for even in the single twitch of a normal muscle the action current is over some time before the muscle has relaxed.

These results bring us no nearer to deciding the exact mechanism of the persistent after-contraction, though they confirm the view that it is of muscular and not of nervous origin. It might be thought that they give some support to the doctrine that the "tonic contraction" differs from a tetanus in that it is not associated with an oscillating electric response. This doctrine has been the subject of much discussion recently [22], and we do not propose to deal with it except to point out that the persistent after-contraction in myotonic muscles need not have anything to do with the long-continued, postural contractions to which the name "tonic" is commonly applied. A discussion of the different factors which may be involved in a persistent contraction of muscular origin is given in a recent paper by Hartree and Hill [23] on "The Mechanism of the Veratrin Contraction."

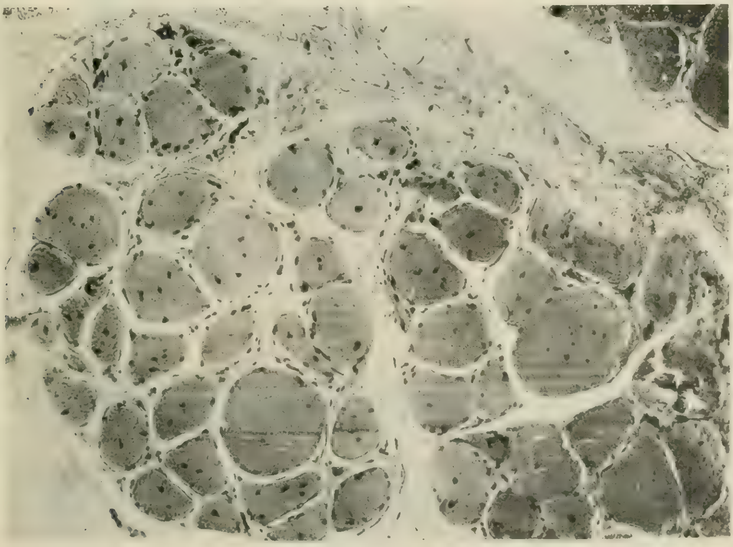


FIG. 4*a*.

Histological examination of a portion of excised muscle.—A piece of the right deltoid muscle removed by open operation was fixed in formalin saline and embedded in celloidin; sections of it were stained with alum hæmatoxylin and van Gieson's counterstain. These sections showed very striking alterations which are illustrated in fig. 4. The fibres were of very varying size, ranging from 8 μ to 150 μ in transverse diameter. On cross-section almost all were of rounded outline, and the connective tissue between the individual fibres appeared to be rather thicker than normal. On longitudinal section some of the fibres showed localized swellings, which were associated with some loss of the transverse striation, and in most of the fibres the longitudinal striation was exaggerated. The sarcolemma nuclei were much more numerous

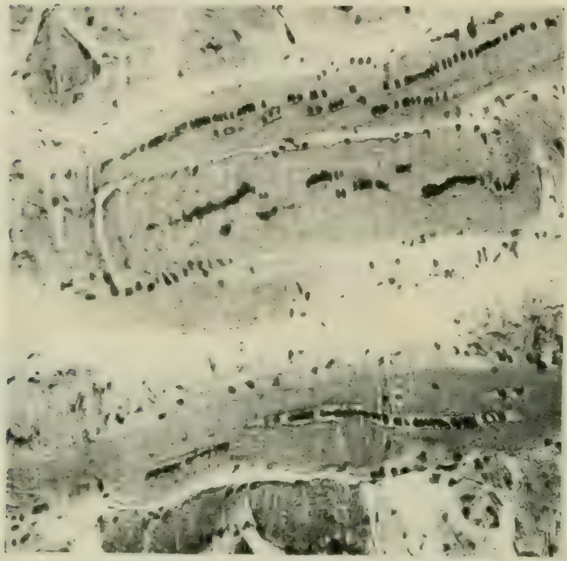


FIG. 4*b*.

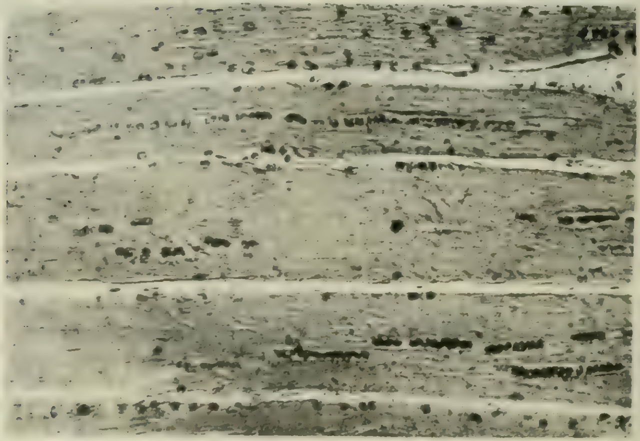


FIG. 4*c*.

FIG. 4 (*a*, *b* and *c*).—*Case* 1. (*a*) Transverse, and (*b* and *c*) longitudinal sections of deltoid muscle. Note in (*a*) internal nuclei and excess of connective tissue between the rounded fibres. In *b* and *c* several chains of internal nuclei are seen, some of which are surrounded by a clear zone.

than normal, and in many places dark-staining nuclear masses lay between the muscle fibres. Many nuclei were also seen within the muscle fibres—in fact, almost every fibre contained some nuclei in its substance. These nuclei were often arranged in chains running down the centre of the fibre.

Three stages of this change appeared to exist: (1) In the first stage the nuclei are elongated and lie end to end, separated from one another by a definite interval, which is, however, much shorter than the length of the nucleus. (2) In the second stage the nuclei are oval or rounded, and lie much closer to one another, so that, although they remain separate, there is no definite interval between them. (3) The third stage consists of the apparent or absolute fusion of the nuclei to form beaded rods, sometimes of considerable length. When the outline of the individual nuclei can be traced, they are seen to be wider than they are long, and either oval or flattened at the opposed surfaces like rouleaux of red-blood corpuscles. In a few instances two such nuclear rods could be seen lying side by side, but in most cases they were single. One or two muscle fibres consisted almost entirely of such a beaded nuclear rod, to which the sarcoplasm formed a very thin covering.

This case conforms to the classical descriptions of dystrophia myotonica given by Batten, Steinert and Curschmann, in almost every respect. With a well-marked facies myopathica and a characteristic alteration of speech there is muscular atrophy of peculiar distribution, greatest in the sternomastoids, the muscles of the forearms and the muscles on the antero-lateral aspect of the legs; active myotonia is most prominent in the hand-grasps, mechanical myotonia is of wider distribution, and a typical myotonic after-contraction on electrical stimulation is present in a few muscles only. There are numerous general dystrophic phenomena, including baldness, atrophy of the testicles with loss of sexual power, loss of body weight, acrocyanosis and increased secretion of tears; all the tendon reflexes in the upper limbs and the knee-jerks are abolished.

Case 2.—John R., aged 31, was admitted to the National Hospital, Queen Square, under the care of one of us, in August 1922, complaining of "difficulty in letting things go" and "stiffness in the legs" of seven years duration. Apart from an attack of influenza in 1917, he was always healthy; prior to the outbreak of the Great War he worked as a hairdresser and played football as a professional. Soon after joining the Army in 1914 he underwent an examination in rifle drill for promotion: during this examination, when he was bent on carrying out the various movements smartly, he suddenly found himself unable to withdraw his hand from his rifle which he had just brought to the slope-arms position, and since then this difficulty in relaxing a firm grasp has persisted. He was not promoted, but his defect did not prevent him from completing his military training and proceeding to Gallipoli, where he was wounded at the landing. After his discharge he returned to his former occupation, but he found that his work was slow and that his earning capacity was greatly diminished; he could work with the scissors fairly well, but the hair-clipping machine caused difficulty because the grip had to be firm. He continued to play football once a week for an amateur team; his game was not so good as it used to be, but he could still "give most of them points," and the old professional enjoyed his game with the amateurs because he was able "to run rings round them." Occasionally when he began to run his feet "buckled up," "the toes turned down and the foot became hollow," "it was a sort of spasm." The spasm was not painful, but he was obliged to stand still for a minute or so until it relaxed. Like the difficulty in the hand, which diminishes with repetition of the movement which caused it, this spasm in the feet was only troublesome at the beginning of a game. He has noticed that if he sits in a squatting position for a few minutes he is unable to rise again without assistance because of "a stiffness in the knees."

His speech is not so clear as it used to be: sometimes when he bites anything hard the muscles of the jaw go stiff, and he often notices a stiffness in the jaws when he chews his food, so that he is forced to masticate slowly; sometimes, too, food sticks in the back of his throat and refuses to go down. He has lost more than a stone in weight during the last year, his hands are always blue and cold. Apart from the troubles already mentioned he has nothing to complain of and feels perfectly well. His father died of diabetes at the age of 61, his mother is still alive and well; one brother, two step-brothers and three sisters are all healthy; all of them have married and two of them have several healthy children. He has a healthy son aged 4. He knows nothing of his other relations

On examination: Height 5 ft. 7 in., weight 9 st. Skull of normal size and form; face very narrow, prominent cheek bones, deep temporal hollows, hollow cheeks, slightly drooping lids, rather thick slightly pursed lips; forehead greasy; large well-formed prominent ears; conjunctivæ not injected, no watering of the eyes; tongue small and deeply wrinkled; palatal arch very high and very narrow; many teeth missing, remainder decayed; no prognathism; hair on head black, marked frontal baldness, thick dark eyebrows, dark beard, shaves daily; thyroid very small; a few dark hairs on the chest, axillary and pubic hair normal in amount and distribution, arms and legs almost hairless; nipples deeply pigmented, skin on neck and upper part of trunk shows uniform brownish pigmentation; testicles very small, especially the left, and very soft, penis large; hands cold and blue, finger nails ridged longitudinally, lunula visible in right thumb-nail only; texture of skin normal, moderate amount of subcutaneous fat.

Heart apex beat in fifth space, ½ in. internal to the nipple line; sounds feeble, pulse regular, 72 per minute, arteries healthy. Urine: specific gravity 1015, contains no albumin or sugar. Lungs healthy. Has great difficulty in getting the bowels to act, abdominal viscera otherwise healthy. Wassermann reaction in blood and cerebrospinal fluid negative. The latter was clear and colourless, contained 3 cells per c.mm., and total protein 0·025 per cent. Nonne-Apelt test negative. Lange 0001110110.

Nervous and muscular systems: Patient is intelligent and well-informed, takes an active interest in passing events and discusses them freely with his comrades; he is rather reticent about his illness and is inclined to resent examination, but it cannot be said that he shows any marked temperamental or psychical defects. Speech is low toned, monotonous and slightly muffled. Vision $\frac{6}{6}$ in both eyes, media and fundus normal, no cataract. Hearing, smell and taste normal. Pupils of moderate size, react well to light and on convergence; range of ocular movements complete, no nystagmus; corneal reflexes brisk and equal; temporal muscles wasted, masseters small and soft, forehead free from wrinkles; slight ptosis of both lids, complete lack of emotional movement of face in conversation, distinct weakness of all the facial muscles in voluntary movement, greatest in the orbiculares oculi; no Chvostek's sign; soft palate thin, does not move well on phonation, palatal reflex present; the tongue is small and deeply wrinkled but its movements are normal; on percussing the edge of the tongue a deep dimple forms and persists for several seconds. The sternomastoids are weak and much wasted; there is no appreciable weakness or wasting of any other muscle. The muscles are moderately firm to the touch and the limbs offer a normal amount of resistance to passive movements. There is no inco-ordination of movement and rapid alternating movements are well performed.

The tendon reflexes in the arms and legs are absent; abdominal reflexes brisk and equal on the two sides; plantar reflexes flexor. No subjective or objective sensory disturbances: sphincters normal. Gait normal, no rombergism.

Myotonia.—Active myotonia is demonstrable in the hand grasps only, the difficulty in opening the hand is greatest at the first effort and diminishes rapidly with repetition; mechanical myotonia: on striking the muscles with a percussion hammer, typical myotonic contractions were obtained in the tongue and in all the accessible muscles of the upper and lower limbs; it was not found in any of the trunk muscles.

Electrical reactions.—To direct and indirect faradism the reactions were normal except for a diminution in the sternomastoids to direct stimulation. To direct galvanic stimulation the response in all the accessible limb muscles was abnormal in that contractions did not occur at make and break only but persisted as long as the current was passing; in the flexors of the forearms the contraction persisted after the stimulus was withdrawn, but in all the other muscles relaxation occurred with cessation of the stimulus.

In this case the diagnosis is founded on the association of muscular atrophy of peculiar distribution—facies myopathica and atrophy of the sternomastoids—with active myotonia most conspicuous in the hand-grasps, reactive myotonia of wider distribution, and a number of general symptoms including atrophy of the testicles, baldness, and acrocyanosis.

Case 3.—Edith B., aged 41, a children's nurse, was admitted to the National Hospital, Queen Square, under the care of Dr. Risien Russell, in November, 1922, for "sudden falls and weakness" of four years' duration. She enjoyed perfect health until four years ago, when she began to "fall to the ground helpless two or three times every day." The attacks, which were regarded as "a kind of fit," came on without warning and without apparent cause; consciousness was unaffected, but the whole body became rigid, and she was quite helpless for a minute or two; she then rose to her feet again, feeling none the worse for the attack. At that time she was "able to walk miles," and she had not detected any weakness in the limbs. This went on for three months; she then went to a doctor, on whose advice she had all her teeth removed; after this the falls became much less frequent.

About a year ago she began to tire easily in walking, and had difficulty in climbing stairs. About the same time she noticed that if she grasped an object firmly, the hand "shut up tightly, and would not open again." Sometimes the right hand closed up of its own accord and remained closed for a minute or more.

Apart from general weakness and the spasms in the hands, she feels perfectly well. She has lost a lot of weight during the last few years; the arms and legs are much thinner than they used to be, and her facial appearance has altered; her hair is falling out freely, her voice is not so clear as it used to be; she has never had a friend of the male sex, and the thought of marriage has never appealed to her; the menstrual periods are still regular; she sees well with glasses; she has never noticed any increase in the amount of sputum, sweat, or tears; the hands are always blue and cold.

She had been very healthy until the present trouble began. Her father died of tuberculosis at the age of 58, her mother of cancer at the age of 76; she has four brothers—two are healthy, but two, one older and one younger than herself, suffer from the same disease as herself. They have the same "woe-begone" expression—one of them cannot close his eyes, and both of them are getting gradually weaker. So far as she knows, they have never had any difficulty in letting things go. She has never heard of any muscular or nervous trouble in any other member of the family, or of cataract.

Condition on examination.—Height 5 ft. 3 in.; weight 6 st.; skull of normal size and shape; ears small, well-formed; face lacks expression, deep temporal hollows, sunken cheeks, smooth forehead, drooping lids, slightly pursed lips, edentulous, very high, narrow, hard palate; hair on head scanty, light brown, becoming grey; axillary and pubic hair normal in amount and distribution, other parts hairless; thyroid gland enlarged and firm, breasts normal; hands cold and blue; nails brittle—"I try to get them long, but they always break off"—no lunulæ; skin healthy, very little subcutaneous fat. Abdominal and thoracic viscera healthy. Blood count: Red blood cells, 5,600,000; hæmoglobin, 100 per cent.; white blood cells, 6,650; polymorphonuclear cells, 59·5 per cent.; lymphocytes, 34·5 per cent.; hyaline, 5·5 per cent.; eosinophils, 0·5 per cent.

The patient is intelligent, has a very good memory, makes an excellent witness, and is a pleasant person, entirely free from the temperamental defects which are so common in this disease. Speech is low-toned, monotonous, and muffled. Hearing, smell, and taste are normal. Vision $\frac{6}{9}$, with glasses right and left.

"In the right eye the periphery of the lens shows a complete ring of dust-like opacities lying mostly anterior, with one or two streaks radiating from the periphery and lying posterior to the ring of opacities. In the left lens the same dust-like opacities and the same radiating streaks are seen." (Mr. Leslie Paton.)

Pupils of moderate size, equal, regular in outline, react well to light and on convergence; range of ocular movements complete, no nystagmus, diplopia, or strabismus. Corneal reflexes present; extreme wasting of the temporal muscles, masseters small, but firm, no difficulty in chewing. Typical myopathic face, with weakness of all the facial muscles, especially the orbiculares oculi; no Chvostek's sign. Soft palate not unduly thin, palatal reflex present, no difficulty in swallowing. Tongue small, movements of good range and power, well-marked myotonic after-contraction on percussion.

The sternomastoids show extreme atrophy, and all the movements of the neck are very weak; when she is lying down, the head cannot be raised from the pillow, and if the trunk is raised passively the head falls back; the muscles of the trunk and of the shoulder and pelvic girdles are small, but not obviously wasted, and their power is retained; atrophy is severe in the forearms and in the small muscles of the hands, and all these muscles are very weak, especially the extensors of the wrists and fingers; in the lower limbs there is severe atrophy of all the muscles below the knee and of the vasti of the thighs; the power of dorsiflexion of the foot is almost lost.

All the tendon reflexes in the upper and lower limbs are present, but they are very feeble; the abdominal reflexes are brisk: the plantar response is normal. No objective sensory disturbance was detected.

Active myotonia is confined to the hand-grasps, mechanical myotonia is present in the tongue, deltoids, and thighs.

The patient walks slowly on a wide base with the eyes directed to the ground and with a definite "steppage" gait.

There is no sphincter disturbance.

Histological examination of a portion of excised muscle.—Pieces of the right deltoid muscle removed by open operation were fixed in 5 per cent. trichloracetic acid, and in 10 per cent. formalin saline solution. The former fixative was employed as being that which Heidenhain used to demonstrate the appearance of coils of muscle fibril round the muscle fibres (*v. infra*). We were, however, unable after prolonged searching to see anything resembling this phenomenon. This fixative seemed to produce considerable swelling of the muscle fibres, and we therefore base our description of the histological appearances of this muscle on sections of the piece fixed in formalin saline. These revealed comparatively slight alterations from the normal. The muscle fibres appeared to be unduly rounded, and the sarcolemma nuclei were definitely increased in number. Many of the fibres contained central nuclei and these were often arranged in chains corresponding to the first stage described in Case 1. But in many fibres no central nuclei could be seen. A few of the fibres were shrunken, stained a browner colour than usual with van Gieson's counterstain, and contained a large number of nuclei within them. The majority of the fibres were of normal thickness, and in none could we demonstrate any loss of the transverse or increase of the longitudinal striation.

Case 4.—The patient came under observation at the National Hospital in 1906 when he was 24 years of age, and was described by Batten and Gibb (Case 5) in their original paper on myotonia atrophica. He died at the age of 39 years in the Infirmary of St. Mary's, Islington, in 1921, and through the kindness of the Superintendant, Dr. Arthur Robinson, one of us was able to perform a post-mortem examination thirty-six hours after death.

Post-mortem examination.—The body was extremely thin and emaciated. There was a rounded kyphosis in the upper thoracic region. The limbs were greatly atrophied, especially below the knees and elbows.

The brain and spinal cord were removed and showed no abnormality to the naked eye. The thyroid gland appeared to be normal. The right lung was adherent to the pleura all over, especially at its apex, and was densely infiltrated all through with recent peri-bronchial tuberculosis. At its apex there was a small tubercular cavity the size of a walnut. The right lung showed some old and recent tuberculosis at its apex but not elsewhere.

The heart was healthy and there was very little atheroma of the aorta. The liver was normal ; the spleen was enlarged and congested but presented no sign of tuberculosis. The kidneys were healthy. The suprarenal glands were of normal size, their cortex in places was of a greyish colour, contrasting with other areas which showed the normal light brick colour ; the medulla was normal. The stomach and intestines showed no abnormality.

Muscles : The sternomastoids of both sides were represented only by a very thin band of fibres just under the skin, which was much smaller than the omo-hyoid muscle. The muscles of the forearms, and especially the small muscles of the hands and the anterior tibial and peroneal groups, were very pale and atrophied. Some of the bundles of the erector spinæ group were also very pale, whereas others presented the normal colour and consistence. The abdominal muscles and the hamstrings were well developed and dark in colour.

Pieces of various organs, muscles and nerves were preserved in 10 per cent. formalin saline solution for further examination.

Microscopic examination.—Sections of the right lung showed the appearances of early tubercular broncho-pneumonia, with only the earliest stages of caseation and very few tubercular giant cells. No tubercle bacilli were found in the sections.

The pituitary gland contained a great excess of colloid in the pars

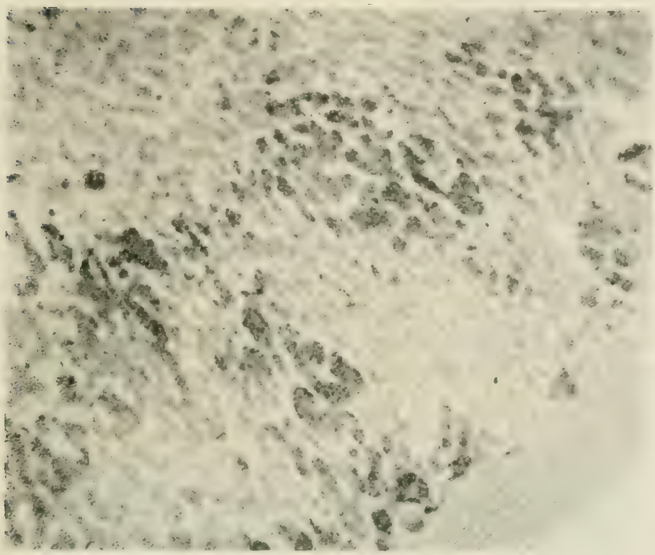


FIG. 5.—*Case* 4. Cortex of suprarenal in Case 4 stained by Scharlach R. and hæmatoxylin, showing the very irregular distribution of the cortical lipoid.

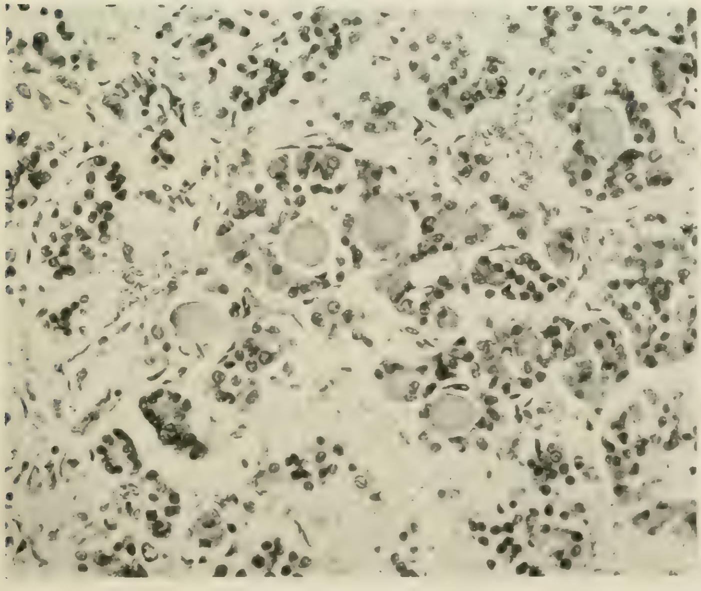


FIG. 6.—*Case* 4. Pars anterior hypophysis in Case 4, showing numerous particles of colloid in the gland acini.

intermedia, and fairly numerous small acini filled with colloid in the pars anterior.

The suprarenal glands showed a very patchy distribution of the cortical lipoid. In places there was none at all, whereas in others it was abundant. The medullary substance appeared to be normal.

Central nervous system.—Sections of brain-stem and spinal cord stained by the Kultschitsky-Pal method for myelin sheaths showed no degeneration either of fibre tracts or of nerve roots. There was certainly no trace of degeneration of the dorsal columns of the cord. Sections stained by toluidin blue showed that the Nissl granules were everywhere well preserved. The motor cells of the cord in the cervical and lumbar enlargements, as elsewhere, were of the normal polygonal shape and their Nissl granules large and angular. They contained no excess of lipochrome.

By hæmatoxylin van Gieson staining there appeared to be slight thickening of the pia-arachnoid in the cervical region, and there was also an excess of small round cells in the dorsal and ventral roots and in the perivascular channels of the larger veins at this level. This change may be probably accounted for by the pleurisy and tubercular broncho-pneumonia from which the patient died.

The sciatic, median and musculospiral nerves stained by the Weigert-Pal (Kultschitzky-Pal) method and by hæmotoxylin with van Gieson's counterstain were found to be healthy.

Muscles : Pieces of muscle from various parts of the body were embedded in celloidin after fixation in 10 per cent. formalin saline solution, and the sections stained by alum hæmatoxylin and van Gieson's counterstain. Some of the muscles showed great change, others little departure from the normal. The latter will be described first.

The biceps flexor cruris and triceps were practically normal. In them the nuclei were confined to the sarcolemma sheath and were not unduly numerous. The fibres on cross section were polygonal in shape and on longitudinal section showed the cross striation perfectly. Some pieces of the erector spinæ group examined were comparatively healthy. In other pieces some of the fibres were thinner and the nuclei more numerous than normal, while others had swollen to about four-thirds of their normal size and showed an excessive number of sarcolemma nuclei both in the sheath and within the substance of the fibres ; these nuclei did not form chains within the fibre such as were seen in more affected muscles. In these large fibres the transverse striation was less apparent and the longitudinal striation more apparent than normal.

Some parts of the sartorius were normal, with the exception that they contained here and there groups of fibres of rounded outline which were furnished with an undue number of sarcolemma nuclei ; other parts consisted of only a few rounded muscle fibres lying together in the middle of fatty tissue. In these fibres the sarcolemma nuclei, although excessive, were almost all confined to the surface.

The sternomastoid showed an analogous condition. Those parts of the muscle which remained appeared practically normal. In other parts no muscle fibres were present, their place being taken by connective tissue and fat, but it was clear from the number of nerves and small arteries, and from the occasional presence of a muscle spindle, that the tissue had originally been muscle. Between the healthy muscle and the areas from which it had disappeared there was a zone in which the muscle fibres became more and more sparse, until only single rounded fibres were found in an area of connective tissue and nerve fibres. This gradual transition made it clear that the healthy muscle was really the sternomastoid and not, as at first appeared possible, a piece of overlying platysma which had been included with the sternomastoid.

The peroneal group showed no gross atrophy of the muscle, but there were definite changes in the muscle fibres. Most of them were fairly large and some were swollen up to 100 μ and 120 μ, which was the largest fibre measured in any muscle in this case. In these large fibres the cross striation was usually poorly marked but still apparent, and on cross section many of them showed clear or relatively pale central areas. Some such fibres had broken up into leashes of thin fibres.

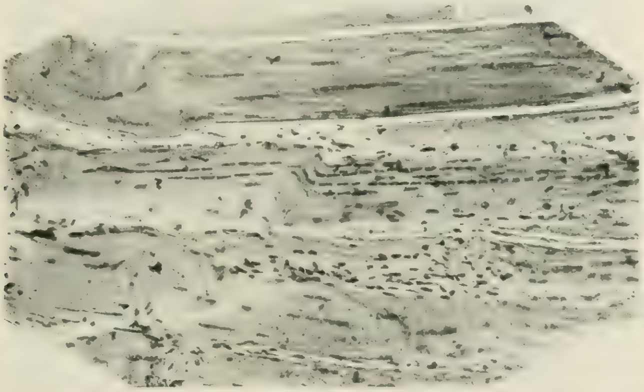


FIG. 7.—*Case* 4. Longitudinal section of peroneal muscle in Case 4, showing chains of internal nuclei.

Many of the muscle fibres in this group of muscles contained chains of nuclei similar to those described in the deltoid muscle in Case 1. The majority of these chains corresponded to the first stage as there described, a smaller number approximating to stage (2).

The tibialis anticus and long extensors of the toes were almost completely atrophied. In only one or two places were there small groups of medium-sized rounded muscle fibres lying singly in the connective tissue. Most of these fibres showed a few central sarcolemma nuclei, but none on the outside of the fibre. It was only possible to trace the origin of the rest of the tissue from muscle by the excessive number of small nerves and blood-vessels which it contained, and by the occasional presence of a muscle spindle near these. The latter, although preserved more than the muscle fibres, were for the most part atrophied to some extent, showing only one or two fine muscle fibres in an overgrown ring of connective tissue. One perfectly normal muscle spindle was found, however, in an area from which all the muscle fibres had disappeared. This group of muscles undoubtedly showed the greatest degree of atrophy of any examined in this case.

In the flexor sublimis digitorum most of the muscle fibres were preserved, but showed great variation in thickness. The largest seen measured 75μ, and numerous thin fibres which appeared to arise by longitudinal fissuring of the larger fibres were present. The sarcolemma nuclei were in great excess, and central chains of nuclei similar to those seen in the peroneal group were very abundant and striking. In some places the nuclei of the sheath were proliferated to form dense purple masses between the muscle fibres (fig. 9, *b*). In a few of the muscle fibres the cross striation was less apparent than normal, but this change had no relation to the number of nuclei either in or within the sheath.

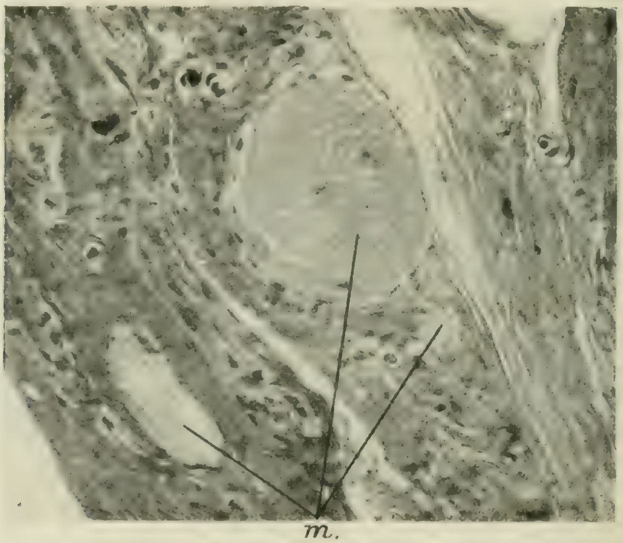


FIG. 8.—*Case* 4. Transverse section of tibialis anticus muscle in Case 4, showing a few muscle fibres (*m*) persisting in the midst of dense fibrous tissue.

The small muscles of the thumb normally contain a considerable amount of fibrous tissue between the muscle fibres, but in this case the fibrosis appeared to be excessive, so that most of the fibres were rounded and isolated from one another by fibrous tissue. Some of the fibres showed longitudinal fissuring, and in a certain number central chains of nuclei were seen, but these were not so numerous or so long as those in the peronei and the long flexors of the fingers. The largest muscle fibres seen in this group measured 75 μ, the smaller ones measured 20 μ or less. In places the muscle fibres appeared to be replaced by fibrous tissue. A few muscle spindles were present in these areas of atrophy, but they were very scarce and difficult to find.

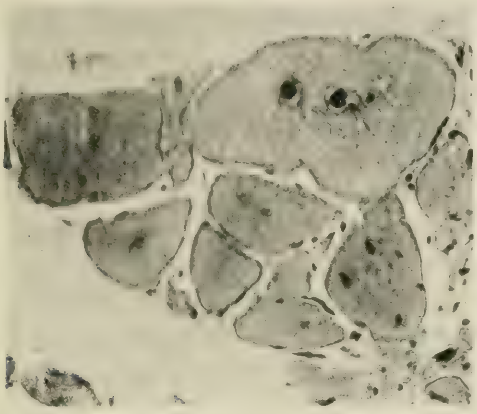


FIG. 9*a*.

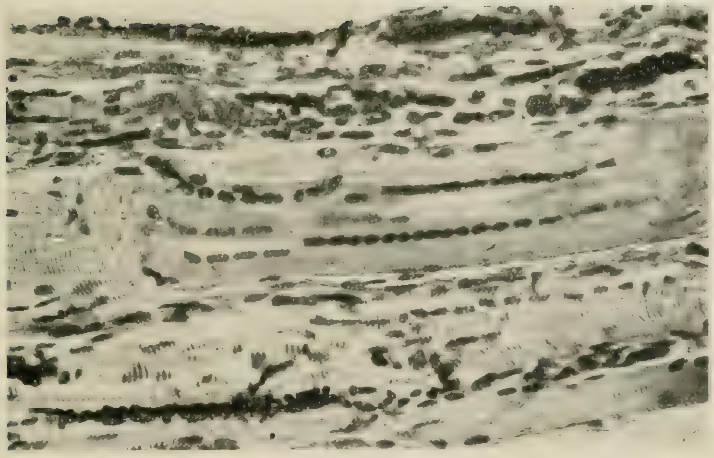


FIG. 9*b*.

FIG. 9 (*a* and *b*).—*Case* 4. Sections of flexor sublimis digitorum muscle in Case 4. In (*a*) a large fibre with large internal nuclei is seen in transverse section. In (*b*) similar internal nuclei are seen in longitudinal section, and there are dense collections of nuclei between the muscle fibres.

III.—GENERAL DESCRIPTION OF THE DISEASE.

Onset and Course.

The age of onset is usually between 20 and 35 years; occasionally it occurs in the late 'teens and in rare instances even earlier; Hauptmann [25] and Grund [20] have each described a case in which symptoms appeared at the age of 10 years.

In a surprisingly large number of reports the statement is made that the patient had been unusually proficient in athletics or gymnastics. One of our patients was a long-distance walker, another a professional footballer; this seems to prove that in some of the cases at least the muscles are perfectly healthy during youth and early manhood. The mode of onset varies greatly; in many instances it is insidious, coming on without any apparent exciting cause and the patient is unable to set a date to the first appearance of his trouble; in others, especially when some form of myotonic disturbance has been the first symptom, the onset is sudden and dramatic and its exact date is known. In a number of cases some feverish illness has served to disclose a weakness of the muscles that had not been noticed before; in our first case and in cases described by Batten, Rossolimo, Hoffmann, Curschmann, Rohrer, Rülf and others, severe pains in the limbs have been a conspicuous feature in the early stages; the nature of these pains is obscure but they are certainly frequent, and although they have not received special mention by previous writers it seems to us that they might well be included amongst the characteristic features of the disease.

According to Rohrer's statistics the first subjective symptom has been myotonia or weakness in about an equal number of cases, but this does not decide the old question of priority of symptoms, for objective examination often discloses the presence of one or the other, although it has given rise to no subjective disturbance. In our patient, J.R., myotonic symptoms have been present for seven years and although there is atrophy of the face and neck muscles the limbs are strong and he makes no complaint of weakness; other cases have been described in which myotonia has preceded weakness by an even longer interval. Moreover, undoubted cases of dystrophia myotonica have been described in which myotonia was a prominent symptom whilst weakness and atrophy were entirely absent; in some cases then myotonia certainly appears first. Those who oppose the contention that it always appears first, and practically every modern writer on the subject is included in this category, base their opinion on the findings in a few advanced cases in which myotonic signs could not be demonstrated at the time of examination of patients who gave no history of myotonic symptoms; but many patients in whom myotonia can be demonstrated objectively have never had subjective symptoms; objective myotonia is notoriously variable, and it tends to disappear in the late stages when atrophy is severe; absence of myotonia therefore has not the same evidential value as absence of atrophy, hence we conclude that myotonia certainly appears first in some cases and probably in all, whereas there is no proof at present that it may be preceded by muscular atrophy. Further reference to the site and mode of onset of muscular atrophy and myotonia will be made in the following chapter.

The course of the disease is usually extremely slow; our patient, W. A., however, was severely incapacitated within a year of the onset, and the same rapid course was observed by Hauptmann in a man who had served in the trenches for a long period during the Great War; within a year of the onset weakness and atrophy were widespread and severe. Life is rarely prolonged after the 45th year; the oldest patient in the records is one of Oppenheim's who lived to the age of 50. Tuberculosis has been named as the commonest cause of death; it was the cause in our patient F. W., but Fleischer denies that it is common; in many cases death seems to have been the result not of intercurrent disease, but of that curious "asthenia" which so often supervenes in chronic disease of the muscular and nervous systems.

(2) *Muscular Atrophy and Myotonia.*

An examination of a large number of patients suffering from dystrophia myotonica, with special reference to the extent and intensity of muscular atrophy and myotonia, reveals the fact that these show considerable variations. At one end of the series there are cases in which atrophy is widespread and severe and many muscles are myotonic; in an intermediate position there are many in which one is severe whilst the other is slight, or both are present in a minor degree, and every gradation is encountered until we come to the rare cases in which one or the other is absent. Hence, although a bare knowledge of the facts that muscular atrophy is usually found in the face, neck and forearms, and that myotonia is usually present in the hand-grasps, will enable the observer to recognize typical cases, a much more profound knowledge is necessary if the numerous cases that diverge widely from the classical Batten-Curschmann type are not to escape detection. It might be thought that the severity of the symptoms would depend on the duration of the disease, but this is by no means the case.

Myotonia.—From its former position as the primary and essential symptom of the disease myotonia has been relegated by general consent to a rank equivalent with the other cardinal symptoms; and certain authors (Curschmann, Rohrer, Naegeli) have attempted to place it in an entirely subordinate position. Nevertheless, we place it first because it is certainly the most constant symptom, and because, in our opinion, it still holds its place as a most important feature of the disease. The slow relaxation of muscular contractions that constitutes the symptom may occur after active movements, or after contractions elicited by mechanical or electrical stimulations; as a rule it is present in more than one form, some muscles perhaps showing it to one kind of stimulation, some to another, but it may be present in any one form alone. All writers agree that active myotonia is shown most frequently by difficulty in relaxing the hand-grasps; in many cases it is confined to this part, but this feature, characteristic as it is, has been given undue prominence in current descriptions of the disease. Hauptmann, for example, is inclined to suspect the diagnosis when active myotonia is present in many muscles other than those of the forearms, but a number of undoubted cases have been described in which many muscles showed this sign. In our patient, J. R., the difficulty in relaxing the grasps, the "buckling up" of the feet on beginning to run, the stiffness in the knees after squatting, and the stiffness in the jaws during mastication, are all expressions of active myotonia. In the patient, W. A., it is demonstrable in all the limb muscles, and in this patient as in others described by Tetzner [56], Rohrer [46], and Rülf [49], the impression was gained that all the muscles of the body were more or less myotonic.

Hence, whilst it is true that active myotonia is most obvious both to the patient and to the superficial observer in the hand-grasps, we feel sure that a careful consideration of all the symptoms and the application of appropriate tests will disclose the fact that it is of much wider distribution in a large proportion of the cases.

As a rule, the difficulty in relaxing the grasp comes on very gradually, and the patient may be unable to state definitely when he noticed it first; but in our patient, J. R., and in another described by Rülf, the onset was sudden, and the spasm reached a maximum degree at its first appearance.

The delay in relaxation usually diminishes rapidly with each repetition of the movement, so that after several attempts it disappears, but several cases have been described in which it persisted or increased. The trouble is always greatest in cold weather, and emotion plays an interesting part in its production. Thomsen himself referred to the effects of psychical stimuli upon a myotonic patient, and the power of these stimuli to provoke the first and subsequent attacks of muscular spasm in persons presumably myotonic from birth is exemplified in the cases of Thomsen's disease so admirably described by Rosett [47] in a recent number of this Journal.

That the same phenomenon occurs in the so-called symptomatic myotonia of dystrophia myotonica is shown by the circumstances in which it appeared for the first time in one of our patients (J. R.); here the emotional factor was provided by the desire to excel in an examination in rifle drill for promotion to higher military rank; prior to this ordeal the man had never experienced any difficulty in relaxing his grasp, but at a critical moment the flexors of the forearm went into severe spasm, with the result that he was unable to remove his hand from his rifle for several seconds.

As in Thomsen's disease, the severity of the spasm in these cases depends on the amount of power that is put into the movement. One of our patients told us that he always knew when attempts to demonstrate the myotonic hand-grasp would be successful, but it transpired that what appeared at first to be an inexplicable premonition was merely artfulness on the patient's part; for at times when he was not disposed to encourage curious visitors, he abolished his most interesting symptom by the simple expedient of refraining from exerting the amount of strength which he knew from experience was requisite to elicit it. Still another similarity with Thomsen's disease must be mentioned, namely, the sudden "falling like a log" of which some patients with dystrophia myotonica also complain. Rosett relates that this symptom was first described by Charles Bell in 1837, before Thomsen's disease was recognized as a definite entity, and he records its occurrence in two of his own cases. In three of our patients these falls were a prominent symptom; we attributed them at first to weakness in the thigh muscles, but on consideration it seemed that this should not cause a man walking on level ground or, as in one instance, a sentry standing at his post, to fall "like a log," and we were at a loss for a satisfactory explanation. On learning that these falls occur in Thomsen's disease, however, we concluded that they were an expression of myotonia in this disease as well. We realize that the falls are indeed due to weakness in the thighs in many instances, but we are convinced that this is not the explanation in all. Occasionally, when weakness causes a patient to stumble, the effort to prevent a fall causes a generalized spasm of the muscles, so that the patient lies rigid on the ground and except that consciousness is retained appears to be in a fit. In one case this kind of attack was mistaken for a seizure of general paralysis.

In several of our cases we have noticed that alternating movements, flexion and extension at the elbow, for example, were well done if the patient was allowed to carry them out at his own rather slow pace, but that if he attempted to increase their rate they became grossly incoordinate, the most obvious defects being that one movement, say extension, was begun before flexion was completed, and vice versa, and that adventitious movements were made at the shoulders and wrists, so that after a number of repetitions the arms were flung about in a most disorderly fashion, the desired movement of flexion and extension being but little in evidence. This phenomenon finds a ready explanation in the myotonia of the muscles involved; when the movements are carried out slowly one group of muscles has time to relax before contraction begins in the other; but when the patient attempts to increase their rate, in the first place he exerts greater force, so that myotonia is more likely to appear, and in the second relaxation is not complete in one group before contraction begins in the other. Rosett has shown in cases of Thomsen's disease that if a stimulus to myotonic muscles, be it mechanical, electrical or volitional, is repeated rapidly, a summation of residual contractions occurs; it may be then that in our cases as well, after several repetitions of flexion and extension, the muscles concerned in these movements, agonists and antagonists alike, go into continued contraction, so that ultimately neither flexion nor extension is possible. But the patient is still exerting himself, and an overflow occurs to muscles moving other joints, so that irregular adventitious movements occur.

Having drawn attention to these expressions of widespread myotonia it is perhaps necessary to repeat that, although this symptom may be demonstrable in many muscles, it is true that in the great majority of the cases it is *obvious* in the hand-grasps alone.

Contrasted with the limited distribution of obvious active myotonia, persistence of contractions produced by percussion of the muscles—mechanical myotonia—is usually more widespread. It is most constant in the tongue and in the small muscles of the thenar and hypothenar eminences, but it is often present in many other muscles as well. In the tongue it is sought for by striking the lateral border with a small percussion hammer; when it is present a deep dimple forms at the point of impact and persists for several seconds; in the hands it is even more easily demonstrated because the prolonged contraction of the muscle is associated with obvious and prolonged displacement of the thumb or little finger, according to the part that is struck. In larger muscles the characteristic myotonic response to mechanical stimulation is the formation of a persistent furrow deepest and broadest at the point of impact. Mechanical myotonia, like other forms of myotonia, varies greatly in the extent of its distribution in different cases, and it shows great variations in the same case at different times.

It is always most obvious in muscles showing little atrophy or none at all, and it is rarely found in wasted muscles; but this cannot be accepted as evidence of an antagonism in distribution between atrophy and mechanical myotonia as some have held, for we have frequently seen mechanical myotonia in the as yet unwasted muscles in parts where atrophy is common. We find the explanation of the apparent antagonism in the fact that mechanical myotonia disappears when atrophy supervenes. When atrophy is absent in muscles where it commonly occurs, these muscles are frequently myotonic; in cases with atrophy in the usual situations myotonia is absent in the wasted muscles but is found in muscles free from atrophy; in advanced cases when all the muscles are wasted, mechanical myotonia may be nowhere demonstrable.

Before leaving this subject something must be said of a kind of persistent contraction after mechanical stimulation which has nothing to do with myotonia. The normal response to mechanical stimulation is a contraction of short duration in the long axis of the fibres beneath the point of impact; now it often happens that as the fibres relax in parts remote from the point of impact a prominence appears at this point, and after persisting for several seconds disappears slowly; this can be observed most easily in the pectoral muscles, but may be present in many others; the duration of this localized transverse swelling is often just as great as the persistent contraction of myotonic muscles, and may cause confusion, but error will be avoided if it is remembered that the true myotonic reaction appears in the form of a dimple or furrow, not as a prominence.

It has been stated that the normal myotatic irritability of the muscles is abolished in this disease. In a number of our cases we have investigated the response to mechanical stimulation in all the accessible muscles, and we have been struck by the frequency with which such stimuli failed to produce a response of any kind in muscles that seemed to be healthy in other respects; nevertheless, normal responses were often obtained, and in several cases percussion of the pectoral muscles evoked a typical "harp-string response" (Oppenheim) which did not differ in any respect from that seen in normal individuals.

Electrical Reactions.

The electrical reactions in this disease show many deviations from the normal: the quantitative changes are those that we expect to find in muscular atrophy of myopathic origin; the qualitative changes are identical in nature with those that occur in the myotonic muscles of patients with Thomsen's disease, but are often modified by the presence of atrophy in the myotonic muscles. In weak muscles and muscles showing active or mechanical myotonia, the reaction to direct faradic stimulation is often diminished; as a rule the reaction to indirect faradism is normal, but when atrophy is severe this is also diminished; to direct galvanism the excitability of the atrophic muscles is sometimes increased, but it is more often diminished. In many respects the reactions resemble the reaction of degeneration, for apart from the changes just mentioned A.C.C. is often greater than K.C.C. and slow worm-like contractions are sometimes observed on direct galvanic stimulation; indeed the earlier writers described their findings as a combination of the myotonic reaction with the reaction of degeneration. Steinert and Curschmann, however, pointed out that the slow contractions only occurred on closing the current, whereas anodal opening contractions were prompt; that even the closing contractions become normal on repetition of the stimulus, that slow contractions may occur on direct faradic stimulation also, and that the muscle is usually excitable through the nerve. Their conclusion was that the changes were merely deviations of the myotonic reaction due to the presence of atrophy in the muscles and that they differed fundamentally from the reaction of degeneration. With this view almost every subsequent observer has concurred, and we may safely conclude that the reactions in this disease, however closely they may resemble it, have nothing to do with the reaction of degeneration whatsoever.

In most cases the classical myotonic reaction is found in very few muscles or in none at all, but it is usual on the other hand to find changes in many muscles which may be looked upon as minor modifications of it. In some cases no normal twitches can be obtained from some of the muscles by direct galvanic stimulation, for even with minimal current strengths the muscle goes into a prolonged tetaniform contraction; this constitutes Remak's "incomplete myotonic reaction." In others galvanic and faradic stimuli of short duration evoke normal twitches, but if the stimulus is prolonged, the strength remaining the same, a myotonic after-contraction occurs (Steinert-Pässler phenomenon). This type of reaction was present in two of our cases; in some muscles the contraction persisted as long as the current was passing and relaxed promptly as soon as it was withdrawn, in others relaxation was slow; with the galvanic current this phenomenon occurs more readily from the anode than from the cathode. In cases described by Steinert, Hauptmann, Baake and Voss, and Maas and Zondek, no response was obtained from some of the muscles with currents of minimal strength, but when the stimulus was greatly prolonged the strength remaining the same, the muscle went slowly into continued contraction and then relaxed slowly after the stimulus was withdrawn. This type of reaction was seen in one of our patients; we observed that during the slow inception of the muscular contraction the galvanometer needle was rising and that as long as the needle remained steady the muscle remained in "galvanotonus." We concluded therefore that the phenomenon was due to "galvanotonus," and that the appearance of the slow contraction was due to a gradual diminution in the resistance of the skin. Many other modifications of the classical myotonic reaction have been described, indeed it seems as if every observer who directs his attention to the electrical reactions in these cases finds something that has not been described before, but it is not yet possible to say whether any one of them is constant or peculiar to this disease.

We have said that myotonia is the most constant symptom of the disease; we must now consider the cases in which it was said to be absent.

Under the heading "Dystrophia myotonica sine myotonia," Curschmann [10] has described a family consisting of three brothers and a cousin; the patients showed muscular atrophy of typical distribution, cataract, atrophy of the testicles, impotence, baldness, loss of reflexes, hypersecretion of sweat and other characteristic symptoms, but in two of them myotonia was completely absent and in another it was present in a minimal form as mechanical myotonia in the tongue and thenar muscles alone. There is no doubt about the diagnosis in these cases, as the patients with and without myotonia but with other symptoms in abundance were brothers. Rohrer has described two cases in which myotonia was absent. In one, a man aged 53, the findings were: atrophy of the forearms, face, sternomastoids, temporals and legs, presenile cataract (operation) at the age of 40, baldness, impotence, general loss of body weight and other less definite symptoms; no myotonia, no history of muscular disorders or of cataract in other members of the family. In the other case, a woman aged 39, the symptoms were atrophy of the forearms and face, presenile cataract and certain indefinite dystrophic symptoms; no myotonia and no family history. In many respects these cases are typical enough, but we hesitate to accept them, as confirmation of the diagnosis from the family history is lacking. Until special investigations have shown that cataract does not occur in other muscular dystrophies, we cannot agree that the combination of presenile cataract with muscular atrophy but without myotonia justifies a diagnosis of dystrophia myotonica, although it makes it highly probable. It might be said that in Rohrer's cases the diagnosis is confirmed by the presence of other dystrophic phenomena, but we do not attach much importance to these in doubtful cases, firstly because it has not been shown that they do not occur in other muscular dystrophies, and secondly because the enthusiastic investigator of the ductless glands rarely fails to find evidence of some disorder in their supposed functions in any given case.

In one of Fleischer's cases there is no account of myotonic symptoms, but as the electrical reactions are not given, and as electrical myotonia may be present alone, the case is not acceptable for our present purpose. In some of Batten's original cases too, myotonia was said to be absent, but the investigations, according to modern standards, were incomplete. Against Curschmann's cases, however, there is nothing to be said; they prove that myotonia may be completely absent in isolated cases *at the time of examination*, but they do not permit us to assume, as Curschmann, Rohrer and Naegeli have done, that it may be absent in certain cases throughout the course of the disease, nor do they justify the contention that myotonia is merely an occasional and unessential symptom of subsidiary importance.

Myotonia is notoriously variable in distribution and intensity in the same case at different times; it tends to disappear in the advanced stages when atrophy is severe and general, and it may be absent at one time and present at another, as is shown by the case reported by Niekau [42] as an example of "dystrophia myotonica sine myotonia" which was recognized by Slauck [52] as one that had been under his observation on four occasions when myotonia was always present: we are prepared then to encounter cases in which myotonia is absent at the time of examination, but nothing that we have learned in our study of the disease leads us to associate ourselves with those who hold that it may be absent throughout its course.

Further, with regard to the diagnosis in cases free from myotonia, it must be remembered that the isolated cases in which it was absent stand alone amongst the hundreds in which it was present in some degree; hence we consider that the greatest caution should be exercised before cases without this symptom are admitted to our category. For the present at least we should use the family history as our criterion and withhold the diagnosis in doubtful cases unless the occurrence of characteristic cases in other members of the family supplied the necessary confirmation.

We do not intend to enter upon a discussion of the theory of myotonia in general, but as our electro-myographic investigations have a bearing on this subject it must be mentioned briefly. The earlier writers on Thomsen's disease were satisfied that myotonia was of myogenic origin; during recent years, however, several observers have supported a neurogenic theory. (Curschmann [9], Albrecht [2], Stocker [55], Gregor and Schilder [17].)

Gregor and Schilder working with the string-galvanometer on cases of dystrophia myotonica found during the myotonic after-contraction oscillations with a fifty per minute rhythm, which they therefore regarded as evidence of a central origin for the myotonia. These authors look upon the myotonic reaction as a proprioceptive reflex—the voluntary contraction produces a stimulus in the muscle itself which calls forth another contraction through the reflex path and so on. Schäffer [50] in a recent paper disagrees with Gregor and Schilder's conclusions and upholds the myogenic theory; he failed to find oscillations suggestive of a neurogenic origin for the myotonic after-contraction in cases of Thomsen's disease, and they were certainly absent in our case of dystrophia myotonica; Schäffer showed too that myotonia persists when the nerve endings in the muscles are paralysed with novocain and when the nerves to the limbs are paralysed by regional anæsthesia. Grund [21], moreover, had previously reported that it persisted in limbs paralysed by intrathecal injection of stovaine. This work suggests that the myotonia of Thomsen's disease is myogenic in origin, and our own limited observations lead us to conclude that the same is true for the so-called symptomatic myotonia of dystrophia myotonica.

Muscular atrophy.—Our knowledge of the distribution of the muscular atrophy in this disease has passed through several distinct phases. The earlier writers, Hoffmann [29] for example, saw nothing distinctive in it and commented upon its apparent irregularity. Batten and Gibb on the other hand suggested that "a characteristic distribution may exist in this disease" and by neglecting the cases in the literature that differed from those that had come under their own observation they were able to differentiate a distinct clinical group in which weakness was confined to the facial muscles, the muscles of mastication, the sternomastoids, the vasti of the thighs and the dorsiflexors of the feet. According to Steinert, who had reached the same conclusion independently, three stages could be recognized in the spread of the atrophy: the muscles of the forearms are first attacked, then those of the face, the sternomastoids and the muscles of mastication; at a later stage atrophy spreads from these sites of predilection and many other muscles are affected; the peronei, he added, might be attacked at any stage. Batten and Gibb based their conclusions on the findings in twenty cases; subsequent observations on hundreds of others show how well they attained their object which was "not so much to discuss the whole subject of myotonia atrophica as to suggest the possibility of there existing a form of myopathy differentiated clinically from the classical type as much by the distribution of the wasting as by the presence of the myotonia," for in a majority of cases the distribution of the atrophy conforms to Batten's description; his precise delineation of the features of characteristic cases served its purpose admirably, and, supported by Steinert's findings, it led quickly to the recognition of these cases as a distinct clinical group. But all cases do not conform to these classical descriptions, which apply to a type only, and it remains for us to indicate the variations that may occur. Our conclusions are based on an analysis of 123 cases in which we were satisfied that the diagnosis was correct.

Weakness always appears first in one of the following situations: the facial muscles, the muscles of mastication, the sternomastoids, the forearms, the vasti of the thighs or the dorsiflexors of the feet; it is usually present in more than one of these groups when the patient first comes under observation but it may affect any one of them first, or most, or alone.

The sequence described by Steinert is certainly not constant, nor is it the most frequent, for our figures show that the forearms are spared in many cases when atrophy in some or all of the muscles of the head and neck group is severe. Our Case 2, with extreme atrophy of the sternomastoids without weakness or wasting in the forearms, illustrates this, and cases with little or no wasting in the forearms with severe atrophy in the head and neck muscles have been described by Batten, Tetzner, Curschmann, Kramer, Bramwell and Addis, Rohrer, Hauptmann and others. On the other hand, atrophy of the forearms alone is rare.

Within the head and neck group it is usual to find some weakness of all the muscles, but one pair often suffers more than another and atrophy may be extreme in one, in the sternomastoids for example, before the others are attacked. Absence of demonstrable weakness in the orbicularis oculi seems to be the rarest negative finding; even when this is absent the face is usually described as being "expressionless and immobile"; absence of weakness in the sternomastoids is next in order of rarity. The muscles of mastication usually succumb early; the wasting is always most obvious in the temporal muscles, where it may be extreme before the bulk or power of the masseters is diminished, and the resulting temporal hollow aids materially in producing the characteristic facies of the disease; dislocation of the jaw as a consequence of weakness in these muscles was noted first by Nonne; it occurred in two of our cases. In the forearms the supinator longus is picked out first and it may waste greatly before other muscles in the forearm group are attacked (Steinert, Tetzner, Hauptmann).

It has been said that the extensors are always more affected than the flexors, but our observations suggest that no rule can be given on this point; we have seen several cases in which the flexors suffered most and the same has been noted by Grund, Hauptmann and others. Weakness and wasting of the dorsiflexors of the feet is mentioned in less than half of the cases in the literature, but if our remarks had been founded upon our own observations alone we should have placed the incidence of weakness in this group at a much higher figure. If the lower limbs are attacked at all these muscles or the vasti of the thighs always succumb first; in many cases weakness in the legs has been the first symptom and in some dropped foot and great difficulty in walking were obtrusive symptoms when power in the upper limbs was still good.

From the sites of election already mentioned atrophy may spread to adjacent muscles, or pick out individual muscles at a distance in an order for which we can find no rule; if we were to give priority to any muscles outside the classical situations, we should mention the small muscles of the hands, the deep neck muscles, and the muscles of the upper arms and thighs. In many cases some of these are attacked before atrophy has appeared in all the sites of predilection; for example, when atrophy in the forearms is severe the small muscles of the hands or the muscles of the upper arms may waste before the legs are affected, but no case has been described in which atrophy appeared first in a muscle outside the main groups. The rate at which atrophy progresses is extremely variable; it may be severe and widespresd a year after the appearance of the first symptom, or it may be minimal in most of the muscles many years after the onset of the disease; in one of our patients with wasting of the sternomastoids and facies myopathica the limbs retain their bulk and power seven years after the onset. In some advanced cases every muscle in the body is wasted, in others of equally long duration the trunk muscles and the muscles of the shoulder and pelvic girdles retain their bulk.

As in other types of myopathy, the loss of power in some of the muscles is often greater than the degree of atrophy would suggest; pseudohypertrophy is said to occur in rare cases, but a special study of the recorded cases leaves us in doubt upon this point, as we are inclined to attribute the apparent hypertrophy to the striking contrast in the size of muscles free from atrophy with those that have wasted. Batten described hypertrophy of the muscles below the knee in one of his cases, but the vasti were completely atrophied; in a case described by Griffith, the calves were said to be hypertrophied but their circumference was only 14½ in. and the patient had been a footballer. Slauck mentions that he has seen a case with marked hypertrophy of the quadriceps of the thigh. Mendel demonstrated a case at a clinical meeting in Berlin with typical myotonic symptoms, severe atrophy of the forearms, arms, infraspinati and sternomastoids and "great hypertrophy of the thenar and hypothenar eminences and of the calves," but as there was no facies myopathica, and as extra-muscular symptoms seem to have been absent, the diagnosis is doubtful; we have seen one case that had previously been under the care of two of our colleagues who had both described it independently as one of "myotonia atrophica with pseudohypertrophy"; the contrast between the size of some of the wasted and unwasted muscles was certainly very great, but it was doubtful whether the larger muscles were really hypertrophied. Be this as it may, it is certain that some of the muscles may appear to be unduly large and that these muscles are often extremely weak.

Atrophy of the tongue has been recorded by Grund and Steinert; it was present in two of our cases, but it is uncommon and is always slight in degree.

In two cases described by Albrecht [3] the soft palate was "as thin as paper" and the œsophageal walls were thin and very lax. Various paralyses of the vocal cords have been observed (Nonne [43], Batten [4], Siemerling [51], Bramwell and Addis [7], Albrecht [3], Tilley [57] and others).

Fibrillary tremors identical in appearance with those seen in atrophies of spinal origin were present in the thigh muscles of the patient, W. A., on several occasions; they were seen in one case by Batten and in another by Fuchs, but they were almost certainly fortuitous and all writers agree that they are foreign to this disease.

In certain cases, few in number but of great theoretical interest, muscular atrophy was entirely absent. Case 1 (Rohrer): a woman of 35, with presenile cataract, typical myotonia, expressionless face, nasal voice, no family history. Case 2 (Rohrer): a woman of 36, with typical myotonia, monotonous voice, presenile cataract; two sisters and two brothers suffer from the disease in its most typical form.

Case 3 (Fleischer): a man of 27 with typical myotonia, and incipient cataract; his brother is a typical case. Case 4 (Fleischer): a man of 25 with typical myotonia, apathetic expression, presenile cataract, scanty hair, no family history. Whatever may be thought of the cases in which confirmation of the diagnosis from the family history was lacking, the others prove that the disease sometimes occurs in an incomplete form, and that other symptoms may betray its presence when muscular atrophy is absent. Fleischer's patients were still young and it may be that atrophy will occur later, but both of Rohrer's patients had passed the age at which atrophy usually begins.

So far we have concerned ourselves with the incidence and spread of muscular atrophy; we must now consider its nature. In one particular alone, namely its predilection for the extremities of the limbs, it differs from the better known progressive atrophies of myopathic origin, but in every other respect they are identical; the electrical reactions, apart from the complications introduced by myotonia, are the same; fibrillation is foreign to both, weakness is often great in muscles that have retained their bulk, no changes have been found in nervous structures to account for the weakness and wasting, and, most important of all, the histological changes in the muscles in both conditions are the same and they differ fundamentally from those that occur in atrophies of nervous origin. The morbid appearances in the muscles of four of our patients are described on another page; our findings agree in every detail with those of Slauck [53], whose recent paper came to our notice after the completion of our own pathological investigations; this observer made a special comparative study of the changes in dystrophia myotonica and other progressive myopathic atrophies and found that the agreement was "overwhelming." We may conclude then that the changes in the progressive dystrophies and in dystrophia myotonica are of the same nature, and that in the one as in the other they are, so far as we know at present, myopathic in origin. In other words, the atrophy is not neurogenic in the ordinary sense and does not depend upon a lesion of lower motor neurone. But this does not exhaust the possibilities of a neurogenic origin, for it has been suggested that the atrophy may be due to the loss of a hypothetical trophic influence that normally reaches the muscles through sympathetic fibres. This hypothesis has received warm support from Naegeli and his co-workers, who maintain that the primary defect in this disease is a "pluriglandular disorder of internal secretion"; to explain the muscular symptoms they assume that the functions of voluntary muscles can be influenced through the sympathetic system and therefore indirectly by the ductless glands; striped muscle, they say, identifying themselves with the views of Frank [13] and others, has a double innervation by ordinary motor fibres which supply the fibrils, the part of the muscle concerned in phasic contractions, and by sympathetic fibres which supply the sarcoplasm, the part of the muscle concerned with tonic contractions, and it is to disturbance in the innervation of the sarcoplasm that atrophy and myotonia in this disease are said to be due. A discussion on this alleged dual innervation of the somatic musculature would be out of place here, but as explanations of many obscure phenomena of nervous disease have been based on the assumption that the sympathetic nervous system has an influence on the tone and nutrition of voluntary muscles, we think it should be stated that competent observers in increasing numbers have protested against the unwarranted conclusions to which the possible existence of sympathetic endings in striped muscle have given rise. In the words of one highly qualified observer, the whole subject "still remains within the realms of pure fantasy," and there are many who agree with him. Be this as it may, we must admit that a neurogenic origin for the muscular atrophy in dystrophia myotonica is as yet "not proven," and that in the present state of our knowledge we must look beyond the ductless glands for its cause.

(3) *Cataract.*

Among the many extra-muscular symptoms of dystrophia myotonica cataract holds the place of first importance, not because of its frequency —it occurs in less than half of the cases—but because of the decisive part it has played in the development of our knowledge of the disease as a whole. Its occurrence in this disease was described for the first time by one of us [16] in 1911. In the same year cases were reported by Kennedy and Oberndorf [34], and Ormond [44], and since then others have been described by Kennedy [33], Hoffmann [30], Curschmann [8], Löhlein [38], Hauptmann [24], Rohrer [46], Fleischer [12], Rülf [49] and others.

This curious combination of degenerative changes in structures so dissimilar as lens and muscle at once arrested attention. Greenfield [16] in his original paper was the first to suggest that "the degenerative conditions in the lens and muscles may be due to a deficient vitality on the part of the tissues showing itself in these somewhat specialized structures." In 1912, Hoffmann [30] reviewed the published cases and expressed the opinion that cataract and myotonia atrophica were intimately connected; in the same year, Curschmann [8], seeing in the association of cataract with the other extra-muscular symptoms evidence of a general intoxication, rejected all the pre-existing myogenic theories of the disease, and formulated the hypothesis that it is due to a disturbance in the organs of internal secretion or of the central nervous mechanisms that control them.

Subsequent observations on the incidence of cataract have further enhanced its significance, for increasing knowledge has shown that the other remarkable features first exemplified in Greenfield's family are also characteristic of the disease; we refer to the occurrence of cataract in the otherwise healthy brothers and sisters of patients with dystrophia myotonica, and in otherwise healthy members of earlier generations of the afflicted families. In Greenfield's family five members in the same generation suffered from dystrophia myotonica, two with and three without cataract, and two from cataract alone; a paternal aunt and grandfather also had cataract.

In a family described by Hoffmann, dystrophia myotonica with and without cataract, as well as cataract alone, was found in the dystrophic generation, and a grandfather had cataract. Following these observations, the occurrence of uncomplicated cataract in the brothers and sisters of dystrophic patients was noted with increasing frequency and was soon accepted as one of the features of the disease. With regard to cataract in earlier generations, however, the number of observations remained small (Greenfield, Ormond, Hoffmann); no one ventured to suggest that it was more than a coincidence and no material addition to our knowledge of this aspect of the subject was made until 1918 when Fleischer [12] published a remarkable account of thirty-five cases of dystrophia myotonica with cataract that had come under observation in the eye department of The University Hospital at Tübingen. Fleischer's patients were distributed over twenty-seven families; in eleven of these one of the otherwise healthy parents of children with dystrophia myotonica had cataract, and uncomplicated cataract occurred frequently in the brothers and sisters of the parents and in members of earlier generations.

In one remarkable family, for example, where three brothers and sisters were the parents of children who developed the disease, these three, their younger brother, a sister of the grandfather and a daughter of his sister, as well as the common ancestor, the great-grandfather of the dystrophic generation, all had cataract but were otherwise healthy. To Fleischer's eleven families with uncomplicated cataract in earlier generations we can now add one of Curschmann's [10] with cataract in three members of the dystrophic generation, in four of the preceding generation, and in one of the generation before this.

With all this evidence before us, then, we may now conclude that cataract in earlier generations is also one of the characteristics of the disease. So far we have used the term cataract without qualification; its characters, however, are not the same in the different generations; in patients with dystrophia myotonica and in their brothers and sisters, cataract, if it occurs at all, appears at an early age; in the members of the preceding generation it appears later but is still presenile in most instances, whilst in earlier generations it comes on in old age as ordinary senile cataract.

This remarkable "anticipation" was evident in twelve of Fleischer's families, and is well illustrated in one where cataract occurred in different members of the dystrophic generation at the ages of 27, 30, 31 and 40 years, and in the preceding generation at the ages of 37, 38, 52, 56 and 65 years, whilst a member of the generation before this and his father had ordinary senile cataract. In Curschmann's family the ages were 38, 42, 44 and 47 in the dystrophic generation and 50, 50, 78 and 80 in the preceding generation.

In its typical form the presenile cataract of the dystrophic generation begins as a star-shaped opacity first in the posterior and then in the anterior cortical lamellæ, with or without very fine punctiform opacities scattered throughout the lens. It ripens quickly to a total soft cataract with a small nucleus, at about the same time in both eyes. In the preceding generation its characters are much the same except that consistent with the more advanced age at onset the nucleus is larger and harder. In earlier generations it comes on in old age and has the characters of ordinary senile cataract.

It is not yet possible to say in what proportion of cases cataract occurs; it may be symptomless and, as it is only recently that a special examination of the lens has formed a part of the routine examination of these cases, most of the older reports are valueless for statistical purposes.

The difficulty is still greater in the case of the earlier generations because patients often know very little about their relatives and the opportunity for examining more than a few of them is rarely obtained. Ten years ago Hoffmann estimated that 10 per cent. of patients with dystrophia myotonica also had cataract; Curschmann's estimate (1922) is 30 per cent.; time may show that it is even higher than this.

Of Fleischer's thirty-eight cases with cataract twenty-four were women; this is surprising because the incidence of the disease according to collected statistics is greater in males in a proportion of five to one. Further, most of his patients between the ages of 25 and 35 years were women, whilst those between 35 and 45 were men; and as the other symptoms—muscular atrophy and myotonia—were always found with the cataract his cases seem to prove that cataract is commoner in women, and that not only cataract but also the disease itself appears at an earlier age in this sex.

Some additional points regarding the incidence of cataract will be considered when we come to discuss dystrophia myotonica as a heredo-familial disease.

(4) *Other Dystrophic Symptoms.*

Atrophy of the testicles was noted first by Fürnrohr [15]; next to baldness it is perhaps the most frequent extra-muscular symptom. Its value as an objective sign is not great, as the size and consistence of the testicles varies so much in normal persons, and its presence or absence in a given case will depend on the observer's idea of the normal. There is no doubt, however, that the sexual functions are affected sooner or later in a very large number of cases of both sexes, and it is reasonable to connect the almost constant loss of desire and power in males with changes in these organs. The statement is often made in case reports that the patients have never had intercourse; in some the external genitals remain infantile; celibacy and childless marriages are common. More often the sexual life is normal up to the age of 25 or 30 with normal procreative powers; then as the disease develops desire and power disappear. One of our patients begat a healthy child at the age of 30, four years after the onset of the disease.

Baldness, especially in the frontal region, is very frequent, and in some cases the growth of hair on other parts of the body is scanty. A general wasting of all tissues of the body and a loss of body weight much greater than can be accounted for by muscular atrophy is seen in many cases. It has been stated that this is due in part to a diminution in the calcium content of the bones, and it is probable that this defect plays a part in the production of the spinal and other bony deformities that are sometimes present in advanced cases.

Increased secretion of sputum, sweat or tears, has been a symptom in a number of cases. (Ortleb [45], Hauptmann [25], Curschmann [8] and others). Hauptmann attaches particular importance to this group of symptoms as he sees in it evidence of a disorder of autonomic innervation. In two of our cases we thought at first that the forehead was constantly covered in sweat, but closer observation showed that the moist appearance was due to an excess of natural grease. We have never seen a case in which the secretion of sputum or sweat was increased; in two cases the eyes watered readily, but whether this was due to lagophthalmos or to excessive secretion of tears we are unable to say.

The effects of injections of substances which are supposed to be of value in revealing the state of the autonomic and sympathetic nervous systems, as pilocarpin, atropin, adrenalin, have been investigated in a number of cases with contradictory results. Excessive reactions to pilocarpin have been noted by Hauptmann [24] and Fünfgeld [14], but in one of our cases susceptibility to this drug seemed to be diminished rather than increased; it is certain that these reactions, even if they mean anything, are not constant in this disease and further investigations are necessary before it can be said that they are frequent. Details of the methods in use are given in an article by Fünfgeld [14].

Other occasional findings that have been recorded as evidence of disorder of the ductless glands are: increase in the relative number of lymphocytes in the blood, eosinophilia, increase in the coagulation time of the blood, increase or diminution in the size of the thyroid gland, vasomotor disturbances, especially cyanosis and coldness of the extremities (whatever its significance, this symptom is certainly common), increased irritability of the facial nerve, and others which are supposed to indicate vagotonia or sympatheticotonia.

All these minor signs have been present in some cases and absent in others, just as they would be in the same number of individuals either healthy or suffering from some other disease, and as it is more than probable that the whole subject of the relation of the ductless glands to the sympathetic and autonomic systems will soon be subjected to drastic revision we do not consider that it is profitable to discuss these symptoms in further detail.

Tabetic symptoms.—Loss or diminution of the tendon reflexes in the upper and lower limbs has been noted in a large number of cases; indeed it is extremely rare for all of them to be present. That this should occur when atrophy of the muscles is severe is not surprising, but it often happens that the knee-jerks, for example, are absent when the muscles concerned appear to be healthy. A ready explanation for this was found in the degeneration of the posterior columns described by Steinert in his case which remained for many years the only one that had been examined after death ; but this degeneration was absent in all the cases that have come to autopsy recently, and it seems as if the cause for the loss of reflexes must be sought in the muscles themselves.

Objective sensory disturbances were present in the lower limb in one of Curschmann's early cases, but this has never been found since and we can safely conclude that it was fortuitous. On the other hand, subjective disturbances, in the form of severe pains in the lower limbs, have been described in many cases, particularly about the time of onset of the disease, as in one of our cases and in others described by Batten, Hoffmann, Rossolimo, Curschmann, Rohrer and Rülf.

The peculiar gait of some of the patients with this disease has also been included amongst the so-called tabetic symptoms. The patient fears sudden falls and therefore walks carefully on a rather wide base ; weakness of the leg muscles and a tendency to dropped foot introduces a steppage element ; the extensors of the neck are weak and the head inclines forward so that the eyes appear to be directed towards the ground, and altogether the resemblance to the gait of some tabetics is a close one but it is entirely superficial.

Romberg's sign has been described in one or two cases, but seeing that sensory disturbances are never present, its significance cannot be the same as the true Rombergism of tabes. Sphincter disturbances were noted in several cases but only in the terminal stages of the disease.

Other symptoms.—Considerable attention has been given to the psychical changes in this disease, but it cannot be said that any particular change is constant or characteristic. As all the patients have belonged to the lower classes it is perhaps not surprising that their intellectual attainments have not been high; all our male patients had earned their own living, some of them in trades that demanded a considerable amount of intelligence. In many cases, however, the temperament shows a peculiarity that is rather difficult to define; dulness and lack of interest are perhaps more apparent than real in the majority of cases, as the expressionless face is apt to be misleading.

It is often very difficult to elicit the facts of the family history and sometimes it seems as if they are withheld voluntarily; the patients are often suspicious and mistrustful, resenting examination and refusing to submit themselves to special tests; they leave hospital without warning before the physical examination is completed and they cannot be trusted to present themselves for exhibition at a time that had been arranged. As a rule they are selfish, unsociable and difficult to manage, but they are cunning and shrewd and well able to look after their own interests; some of our patients on the other hand were pleasant individuals, entirely free from psychical defects and peculiarities of temperament.

Speech is nearly always affected. The voice is low, it lacks intonation and has a more or less definite nasal quality. These defects have been attributed to muscular atrophy and to myotonia; perhaps both play a part, as the lips, tongue, soft palate and vocal cords are often weak, and the tongue and perhaps other muscles as well are frequently myotonic.

Stigmata of degeneration are often present. We have been struck by the almost constant presence of a very high, narrow, hard palate in these cases.

Extreme slowness of the heart has been observed in isolated cases (Rohrer, Griffiths, Maas and Zondek).

Maas and Zondek [39] have described three cases in which they found a dilated heart and a definite increase in the As-Vs interval in electro-cardiographic tracings. This observation lacks confirmation; in the one case that we have examined electro-cardiographically the time relations of the events in the cardiac cycle were normal.

IV.—HEREDO-FAMILIAL FEATURES.

In 1916, Rohrer made an analysis of the published cases of dystrophia myotonica and found that it was familial in forty-three cases and non-familial in forty-nine, whereupon he subscribed to the prevalent opinion that the majority of the cases are non-familial. This notion, that in certain diseases some of the cases are familial and others not, is one with which we are familiar, and Rohrer's figures might have served to perpetuate it; fortunately, however, they have been refuted by Fleischer, who has shown that in dystrophia myotonica at least every case is familial, and his work suggests that the same is true for other familial diseases in which isolated cases are supposed to occur. This observer made *ad hoc* examinations of all the available relatives of his patients and undertook the laborious task of tracing the records of his families through many generations in the church registers. His thirty-eight cases were distributed over nine stocks; twenty-nine of the cases were obviously familial, as other children in the family were affected, and in four others the heredo-familial factor was shown in the presence of presenile cataract in one of the parents, so that only five cases remained in which no family history was obtained. In these the investigations were incomplete, or the patients had disappeared, and their families could not be traced. In two families, brothers and sisters alone were affected; in one family three brothers and sisters who had cataract but were otherwise healthy transmitted the disease to some of their offspring; in one family the affected members in two branches had a common great grandfather; in two unrelated families the affected children in two branches of each had a common great-great-grandfather; in two other unrelated stocks, the relationship of the affected members went back to a common great-great-great-grandfather.

Fleischer's figures contrast strongly with those of Rohrer and must be accepted as proof of the contention that when a family history cannot be obtained, it is much more likely that the investigations are incomplete than that the case is non-familial.

It is easy to understand, on the other hand, why so many apparently non-familial cases have been reported. In the first place, the patient's statement that no other member of his family is similarly affected is often accepted as true; but these patients are notoriously untrustworthy on this point, and they often give the impression that they withhold information purposely, sometimes for obvious reasons connected with claims for compensation or pensions, sometimes for no discoverable reason. Hauptmann, one of the first writers to insist on the invariable familial nature of these cases, has discussed these difficulties, and everyone who has had dealings with these patients must have encountered them. An excellent example is furnished by Bramwell [6], who relates that one of his patients went so far as to deny that he had any brothers and persisted in his denials until he was confronted with a photograph of himself and two brothers that had been taken at the hospital some years before. Again, patients of the class in which this disease occurs often know very little of their relatives, especially of their cousins and more distant relatives of the same child rank as themselves, that is in just those members in whom the disease is likely to occur; further, the disease manifests itself during a short period of life only, and a patient who has perhaps known a cousin as a healthy young adult may well be unaware of the affliction that has come upon him later in life. Another difficulty arises from the fact that one or two children alone may be affected in a large family; one child in eight, one in nine, two in fourteen, two in twelve, two in eleven was the incidence in certain families.

But even when one child alone is attacked it is not justifiable to conclude that the case is non-familial, for in one of Fleischer's families, in which one child in eight was affected, the familial factor was disclosed when it was discovered that this patient and another apparently non-familial case had a common great-great-grandfather. In the face of evidence such as this few will have the temerity to maintain that any isolated case of dystrophia myotonica or indeed of any other familial disease is in reality non-familial, and most will be prepared to acknowledge the truth of Hauptmann's dictum that if a family history is not forthcoming either the diagnosis is incorrect or the investigations are incomplete.

Perhaps the most remarkable fact that has been brought to light by Fleischer's genealogical studies is this, that the disease may be transmitted latently through as many as six generations to burst forth suddenly in a number of families at the same distance from a common ancestor. Transmission seems to take place through males and females indiscriminately, but the fully developed disease is more frequent in males. It seems to us, too, that the syndrome we call dystrophia myotonica is confined almost entirely to one generation. The mother of one of Batten's patients had "difficulty in letting things go" all her life, but no account of other symptoms was obtained, and she attained the age of 82, which is almost double the age that has ever been reached by any patient with the fully developed disease. The father of Tetzner's patient had "wasting of the muscles." One of our patients told us that his father "always slept with his eyes open," but was "very healthy and strong." The father of one of Curschmann's patients "walked unsteadily and his speech was indistinct." Four uncles and aunts and the grandfather of one of Rohrer's patients were said to be affected with the same disease, "it ran in the family." We have collected several more similar observations, but in almost every other case report it is stated definitely that the parents and other relatives of earlier generations were free from symptoms suggestive of the disease. Fleischer's records are of the greatest value because particular attention was paid to this point, and his conclusion is that the occurrence of dystrophia myotonica in the ancestors of his patients was not only never proven but was not even probable in a single instance. The rule, however, is not absolute, for Grund [20] has described a mother and two sons who suffered from the disease in a typical form, and Curschmann [8] found it in a father and son. In the present state of our knowledge, then, it seems as if the position is that in the great majority of cases the parents of the dystrophic generation are healthy (apart, of course, from the frequent occurrence of presenile cataract), that in certain instances, as in the one case where the absence of closure of the eyelids during sleep may be accepted as evidence of weakness of the facial muscles, and in Batten's case, where myotonia was almost certainly present, the parents of the dystrophic generation may present some of the features of the disease, whilst in isolated instances the fully developed disease occurs in members of more than one generation.

It is perhaps too early to say that the disease dies out, as it seems to do, with the generation in which dystrophia myotonica occurs; records exist, however, of about one hundred children and of a number of grandchildren of dystrophic patients, and none of these, apart from the exceptional cases of Grund and Curschmann, has shown any sign of the disease.

But although the syndrome that we call dystrophia myotonica seems to be confined almost entirely to one generation the presence of the degenerative heredo-familial disease in earlier generations is often betrayed by other signs, especially by the occurrence of cataract in the generation to which the parents of the dystrophic patients belong, and in the members of still earlier generations as well. In addition to cataract, Fleischer found in his families frequent celebacy, many childless marriages, numerous twin births, a high infantile mortality, a very high birth-rate in early generations, with a low birth-rate in later generations, a dying out of certain branches of the families, a steady decline in the family fortunes from comparative affluence to poverty, all of which he regards as evidence that these families are in the grip of a progressive degenerative disease. He points out further that the criteria for the heredo-familial degenerative diseases, as laid down by Londe, Jendrassik, Higier and Bing, are all fulfilled in that: (1) several members of the same generation are attacked in the same manner (homologous heredity); (2) the disease appears in several members of the same generation at about the same age (homochronous heredity); (3) the basis of the disease is endogenous; (4) the disease progresses steadily from the moment of its appearance. Further, the progressivity in succeeding generations that is seen in other hereditary diseases shows itself in dystrophia myotonica by the occurrence of cataract which appears at an earlier age in each succeeding generation.

Thanks then to these valuable observations of Fleischer upon which we have drawn so freely, we may safely conclude that dystrophia myotonica must be included amongst the typical heredo-familial diseases such as spinal and cerebellar heredo-ataxy, familial cerebral diplegia, Huntington's chorea, progressive neural and myopathic muscular atrophy, Thomsen's disease, familial optic atrophy, amaurotic family idiocy, colour blindness, myoclonus and the rest. Within this group of diseases this most recent addition holds a place of peculiar interest because it supplies a link between two apparently unrelated muscular disorders, in that both myotonia with all the characters of the myotonia of Thomsen's disease and muscular atrophy in nature identical with that of the muscular dystrophies, are found in it together; on the other hand it introduces a new kind of hereditary disorder into this group in the form of general trophic and vasomotor disturbances, cataract, and so on. It remains to be seen whether this kind of disturbance occurs in other forms of hereditary nervous disease, and further research will decide whether an understanding of the nature of dystrophia myotonica will throw any light on the pathogenesis of heredo-familial nervous diseases in general.

V.—PATHOLOGY.

The study of the pathological anatomy of dystrophia myotonica has confirmed the views already set forth as to the nature of the disease without leading us to any new facts as to its ætiology, or definitely settling many questions which are still under discussion. By far the greatest number of observations has been made on the muscle alone, removed at biopsy, and the variations in the stage of the disease and consequently in the degree of alteration in the muscle examined, has led to some confusion as to the interpretation of the changes which were found.

The first complete post-mortem examination was reported by

Steinert [54] in 1909. He found degeneration of the dorsal columns, and dorsal nerve roots in the lumbar region of the cord, with resultant pallor of the column of Goll in the cervical region. The ventral horn cells and ventral roots were normal. He considered the degeneration of the dorsal columns in his case to be due to the chance association of tabes with the muscular dystrophy. Later post-mortem examinations have confirmed this view. Hoffmann [31] in two post-mortem examinations found no sign of disease in the dorsal columns of the cord. Hitzenberger [28] reported a case in which the only pathological change in the spinal cord was disappearance and atrophy of some of the ventral horn cells, especially those of the ventro-lateral group in the cervical region. Fischer [11] examined another case without finding any evidence of disease in the central nervous system. In Bramwell's [7] case Dawson found nothing abnormal except "marked pigmentation of the anterior horn cells and cells of the posterior root ganglia; and amongst these cells very numerous amyloid bodies."

In our Case 4, as has been stated, the spinal cord showed no pathological alterations. We have therefore records of six post-mortem examinations since that of Steinert, none of which showed degeneration of the dorsal columns. Atrophy and disappearance of those cells of the ventral horns which are connected with the atrophied muscles had previously been described in cases of myopathy by Holmes [32], and it is therefore not surprising that a similar find should have been recorded by Hitzenberger in dystrophia myotonica.

Comparatively little attention seems to have been paid to the *glands of internal secretion* in post-mortem examinations. This is unfortunate, as the assumption that the disease arises from a faulty activity of these glands rests up to the present on a purely clinical foundation. In our case there were changes in the anterior and middle lobes of the pituitary body and in the cortex of the suprarenal gland, of a degree which, while not absolutely pathological, was certainly beyond what is usual. Unfortunately the testicles, the thymus, the thyroid and the parathyroid glands were not examined microscopically, as at the time of the post-mortem examination our attention had not been drawn to Naegeli's view of the disease.

The changes in the muscles have been particularly investigated by Martin Heidenhain [26] and by Slauck [53]. The former observer constantly found in cross sections of the muscle a few muscle fibres presenting a narrow zone of cross striation under the sarcolemma.

Such fibres were found also in myotonia congenita, in myxœdema, and in the eye muscles of the dog. Heidenhain considered that the appearance was due to one or more muscle fibrils being coiled round the bundle of fibrils which forms a muscle fibre, and on this he based an ingenious theory of the myotonic phenomenon. But the sparseness of fibres showing this change, and their occurrence in other conditions than myotonia, militate strongly against any such view.

Slauck, while confirming in his earlier work the observations of Heidenhain as to the appearance of the muscle fibres, does not consider that they have any relationship with the myotonic phenomenon; and in his more recent work he states that in several cases of dystrophia myotonica he has failed to find any such fibres. In each of our cases we have searched carefully for the appearance described by Heidenhain without finding a single fibre which answered to his description.

The degree of change in the histological appearance of the muscles in dystrophia myotonica appears to vary with the severity of the wasting, and to have little or no relationship with the myotonic phenomena. Thus M. J. Stewart in his examination of the myotonic muscles in Griffith's case found only very slight alterations. Through his kindness we have recently had the opportunity of comparing sections of these muscles with those removed in our Cases 1 and 2. We were thus able to see in muscles which were removed during life, and which showed the myotonic reaction in a typical form, three stages of the disease process. In Griffith's case the muscles were approximately normal, showing only an excess of sarcolemma nuclei which have very little tendency to invade the muscle fibres. In Case 2 the sarcolemma nuclei were considerably more numerous, and many had invaded the muscle fibres, producing chains of central nuclei. In Case 1 a much more advanced stage of the process was seen. The muscle fibres varied greatly in thickness; the contour of some was irregular and a few showed signs of longitudinal division. The longitudinal striation was exaggerated and the transverse striation less definite than normal, so that it was impossible to say which of the two was the more obvious; and in cross sections the individual muscle fibrils could be clearly distinguished. The sarcolemma nuclei had proliferated enormously, giving rise to dense chains of nuclei both within and along the border of the muscle fibres, and many heaps of similar nuclei lay between the muscle fibres. There was, however, little evidence of disappearance of muscle fibres. The intramuscular connective tissue showed only a slight increase.

In our post-mortem case still greater variations were found between different muscles. Some appeared to be unaffected. Others showed slighter or greater changes of the types just described, while from some the muscular substance had almost completely disappeared, and had been replaced by connective tissue; when this was the case the few remaining muscle fibres retained their cross striation, and presented a comparatively healthy appearance, although they were thinner than normal, and contained many central nuclei.

Slauck [53] in his recent paper has given an excellent description of these changes and their gradations, as shown by the muscles removed by biopsy in six cases of the disease. He considers that while they have a remarkable similarity to the changes found in Erb's classic type of muscular dystrophy, there is, in dystrophia myotonica, a greater tendency to the formation of chains of nuclei within the muscle fibres.

This phenomenon was so striking in many of the muscles which we examined that we have felt justified in considering it as *the characteristic* feature of the muscular atrophy. It is true that in its slighter degrees it is present in many forms of muscular wasting. For example it is not uncommon to find in atrophied muscles chains of elongated nuclei lying end to end, and separated by a slight interval. But the occurrence of twenty or more rounded nuclei touching one another and forming a chain down the centre of the fibre is much less common; and we have never seen in any other form of muscular atrophy the numerous solid rods of nuclear matter running down the centre of the muscle fibre, which formed such a prominent histological feature of our cases.

On the other hand, all the muscles examined in Case 4 did not show these central chains or rods, and in the most atrophied muscles, such as the sternomastoids and the anterior tibial group, they were uncommon. They appear, therefore, to be characteristic especially of the early and middle stages of the atrophic process.

The other histological changes in the muscle which occur both in dystrophia myotonica and in other forms of muscular dystrophy have been well summarized by Slauck. As described by him the disease process affects the whole muscle substance, but picks out certain fibres especially, so that thick and thin fibres are seen lying together. In the earliest stages there is an increase of sarcolemma nuclei round thick and thin fibres alike, though in some fibres the atrophic process does not appear to be accompanied by any increase of sarcolemma nuclei. At a later stage, more definite signs of degeneration appear; the sarcolemma nuclei tend to pass into the centre of the muscle fibre, and become arranged in rows both inside it and along its surface. The muscle fibres lose their polygonal shape and become rounded, and in many of them the muscle substance disintegrates so that only a collection of sarcolemma nuclei remains to mark the place from which a fibre has disappeared. This final disintegration may affect fibres of varying calibre, and not those of the smallest size only. It is usually preceded by an increase of the internal nuclei. These next become surrounded by clear haloes, so that they appear to be nuclei of cells which have invaded the muscle, rather than sarcolemma nuclei. The disintegration of the muscle substance then commences, starting usually in the periphery of the fibres, and soon results in a shrunken muscle fibre crowded with darkly staining nuclei. Along with the degeneration of the muscle fibres there is an increase of the connective tissue between them in which a varying degree of fat deposition takes place, and eventually this fatty connective tissue more or less completely replaces the atrophied muscle. Very frequently in the later stages of the process dichotomous branching of the remaining muscle fibres can be seen. This, according to Slauck, is an ineffective attempt by the healthier fibres to repair the ravages caused by the disease.

Our own observations of the muscles both in myopathy and in dystrophia myotonica agree in the main with this description. In the latter disease we have noticed that the number of internal nuclei is by no means always proportionate to the increase of the sarcolemma nuclei, nor to the degree of disappearance of muscle fibres. Thus in Case 4 the peronei and the long flexors of the forearm showed the greatest number in internal nuclei, but in the peronei there was little if any excess of sarcolemma nuclei on the surface of the fibres; and neither of these muscles gave evidence of much loss of muscle fibres.

The increase of the longitudinal striation was very striking in several muscles in our series, both in those removed during life and in those of our post-mortem case. It was always associated with a diminution in the intensity, and sometimes with complete disappearance, of the transverse striation. In some muscle fibres both longitudinal and transverse striations had disappeared, so that the muscle took on a hyaline appearance. This, however, was not common; it was remarkable that the transverse striation was often preserved even in the finest fibres. In this particular, as well as in the mode of disappearance of muscle fibres, dystrophia myotonica corresponds with the muscular dystrophies and differs altogether from the muscular atrophies of nervous origin.

In the latter the process appears to consist chiefly in a slow progressive shrinking of the width of the muscle fibre, associated with some degree of increase of sarcolemma nuclei ; the transverse striation is lost comparatively early, so that few fibres of less than 25 μ thickness show any trace of it. The shrinkage continues until the sarcoplasm consists merely of a thin thread uniting the numerous sarcolemma nuclei ; at this stage considerable areas of the muscle may show, in transverse section, small rounded fibres of about 10 μ in diameter which are constituted chiefly by a swollen sarcolemma nucleus. In some, at the level of section, the whole width of the fibre is taken up by the nucleus, so that it is not easy to distinguish them from mononuclear cells. Nothing resembling this picture is ever seen in dystrophia myotonica. Where a fibre has recently disappeared its place is marked not by one, but by many sarcolemma nuclei, and many of the muscle fibres in the neighbourhood are relatively thick. And in the areas of greatest atrophy the few muscle fibres remaining may still show their transverse striation.

It is more difficult to compare the increase of connective tissue in the two forms of muscular wasting, as we have never had an opportunity of examining a muscle from which the nerve supply has been cut off for more than three or four years. Such muscles show a considerable increase of connective tissue, especially around the muscle bundles, but also between the muscle fibres. In Case 1 of our series of dystrophia myotonica the disease had progressed for rather longer than this without producing more than a slight excess of connective tissue. In Case 4, on the other hand, where the disease had been in evidence for over fifteen years, the fibrosis in the most wasted muscles was extreme ; but in other muscles, such as the long flexors of the forearm and the peroneal group which were among those affected at an early stage, there was comparatively little excess of connective tissue.

It appears, therefore, that both in the muscular atrophy following loss of nerve supply, and in dystrophia myotonica, the overgrowth of connective tissue is a purely secondary process, and is largely proportional to the degree of atrophy of the muscles.

VI.—CONCLUSION.

Dystrophia myotonica is a disease *sui generis* within the group of heredo-familial degenerative disorders. It forms a link between other well-known members of this group in that two of its cardinal symptoms —myotonia and muscular atrophy—are identical in nature with the same symptoms in Thomsen's disease and the familial muscular dystrophies respectively. At the same time it introduces a new kind of disorder into this group of diseases, in the form of certain degenerative phenomena in parts outside the muscular and nervous systems.

The fully developed disease is confined in the main to one generation —the dystrophic generation as we have called it—where it occurs in some members of a number of families of the same child-rank in relation to a common ancestor.

The members of preceding generations do not suffer as a rule from myotonia or muscular atrophy, but they often develop cataract which appears at an earlier age in succeeding generations, and genealogical investigations reveal evidence of progressive deterioration in some branches of the stock.

In the dystrophic generation itself some members remain healthy, some may have cataract alone, some may suffer from the disease in an incomplete form—one of the cardinal symptoms, say muscular atrophy, being absent; whilst others present the combination of muscular atrophy and myotonia with certain extramuscular symptoms for which the name dystrophia myotonica has hitherto been reserved. As we have seen in the preceding pages, a majority of the latter conform to the classical descriptions of Batten, Steinert, and Curschmann, but a consideration of the foregoing statements shows that these descriptions apply to a type only—to a syndrome which is merely one aspect of an heredo-familial disease with diverse manifestations.

The disease in all its aspects then remains undesignated, but this discrepancy will be removed if the name dystrophia myotonica is transferred to the disease itself from the syndrome to which it is at present applied. For the syndrome, which also requires a distinctive appellation, " dystrophia myotonica, type Batten-Steinert-Curschmann," would suffice.

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IRON IN THE BRAIN.

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THE specific reactions of different parts of the nervous system to disease are well known to the neuropathologist. He is familiar with the varying forms of neuritis due to alcohol, lead, arsenic, and the toxins of diphtheria; the almost exclusive affection of the motor grey matter of the cord in Heine-Medin's disease, and the local predilections of the morbid processes in the brain in general paralysis and in the atrophies of Pick. Though these specificities are not absolute, they enable the clinician to recognize by means of special symptoms the cause of the disease, even when he cannot determine exactly the parts affected.

A reaction which demonstrates specific chemical properties of some centres of the brain cannot fail to be of interest to the pathologist. The iron reaction does so with wonderful clearness. That this reaction reveals the existence of iron particularly in the nuclei of the extrapyramidal motor system, which owing to the researches of Wilson and the Vogts are of particular interest at present, is another stimulus for the neurologist to study it.

These centres perhaps more than any others in the nervous system show the existence of a striking specificity to disease. I may only refer to Wilson's disease and Westphal's pseudosclerosis, in which there is an association of progressive degeneration of the nucleus lentiformis and of the liver; the lesions of paralysis agitans localized in the globus pallidus and substantia nigra; post-encephalitic Parkinsonism with characteristic alterations in the substantia nigra; the affection of the globus pallidus, and in some cases of certain parts of it only, in poisoning by carbonic monoxide, manganese, hydrocyanic acid and after strangulation; the diseases of the putamen described by the Vogts as "status marmoratus" and "status dysmyelinisatus," and the "Kernicterus" of Schmorl.

The iron reaction has the great advantage that it is easily carried out and can be consequently applied to a large amount of material with little expenditure of time. The method which I have adopted in the following research has been developed by Spatz, who has published his

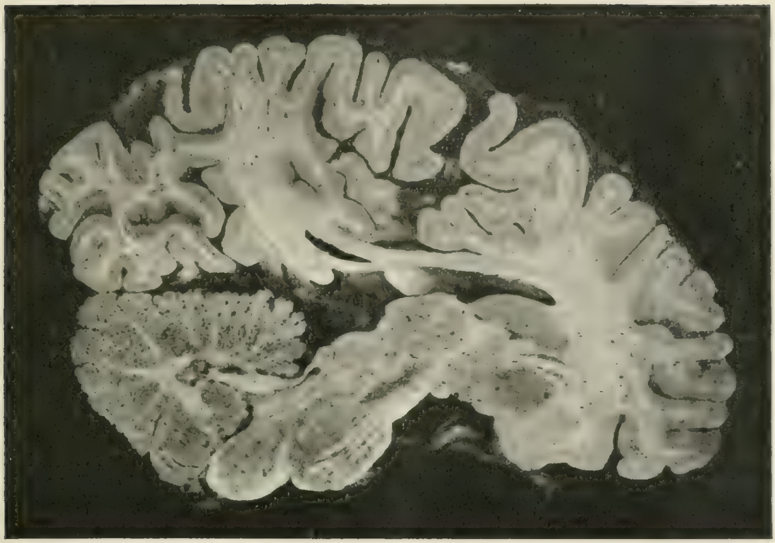

FIG. 1.—Section of a brain which had been fixed for some days in formalin.

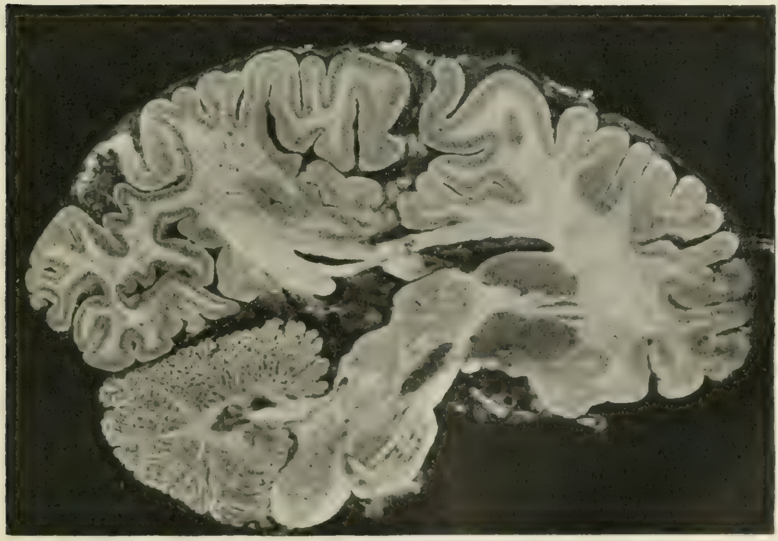

FIG. 2.—The same section as in fig. 1, after being immersed for five minutes in hydrosulphide of ammonium. The substantia nigra and globus pallidus are darkened, and there is a distinct reaction in the nucleus dentatus. The putamen, nucleus caudatus and the lowest layers of the cortex are only slightly darker than before. There is no reaction in the medulla or pons.

own results and brought together the literature on the subject in a recent article [5].

The existence of iron in the nervous system can be demonstrated in either the fresh or fixed state, and macroscopically or microscopically. None of these methods can be neglected, but the most striking results are obtained by examining the fresh brain macroscopically.

A section of the brain is placed in a concentrated deep yellow solution of ammonium hydrosulphide. After some seconds the globus pallidus and the substantia nigra always show a greenish grey colour. It is important to observe the beginning and the order of succession of the colouration, since when they are completed the difference in intensity is not so clear as at first.

After some minutes, when these centres have become dark, other parts begin to react; of these the nucleus ruber shows the strongest reaction, and next the nucleus dentatus cerebelli, the corpus Luysi, the putamen and nucleus caudatus. The difference in the staining of the putamen and of the globus pallidus is of great importance; it is seen most clearly at the beginning of the reaction, but in estimating this difference it must not be forgotten that the putamen has naturally a darker colour (figs. 1, 2, 3). This histo-chemical difference between the globus pallidus and the putamen and nucleus caudatus may be associated with their different ontogenesis and phylogenesis, and with their specific vulnerability; this is seen not only in the rather rare diseases of the extrapyramidal motor centres, for the majority of cases of general paralysis show it with a striking clearness, even those in which during life extrapyramidal motor symptoms were not observed. In the putamen and nucleus caudatus typical cellular infiltrations are found, whilst the globus pallidus is free or nearly free of them, the lamina medullaris externa forming a sharp demarcation (fig. 4). L. Bouman has demonstrated a similar difference in the local distribution of plaques in senile dementia.

In some cases I have found that the nucleus dentatus cerebelli reacted more strongly in its dorsal part. Brouwer [2] has described a case of hemiatrophia cerebelli in which this part was less affected; and from the figure of his paper it seems that in one of Hunt's cases of cerebellar myoclonic dyssynergia [4] this part of the nucleus dentatus was more severely involved. Pathology therefore points out a differentiation in the nucleus dentatus.

Some time after the reaction of the centres of the second group is completed those of the third begin to stain: viz., the corpus mamillare,

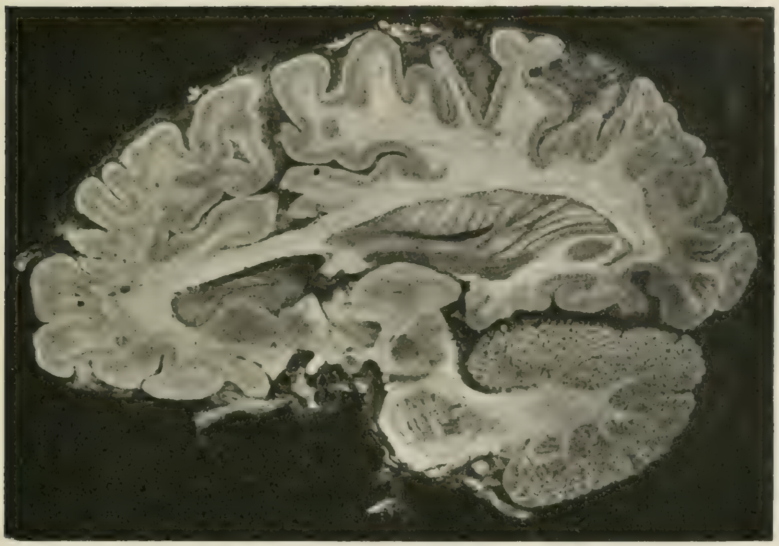

FIG. 3.—The other side of the section in which the nucleus ruber, corpus Luysi and corpus mamillare have taken in the colour.

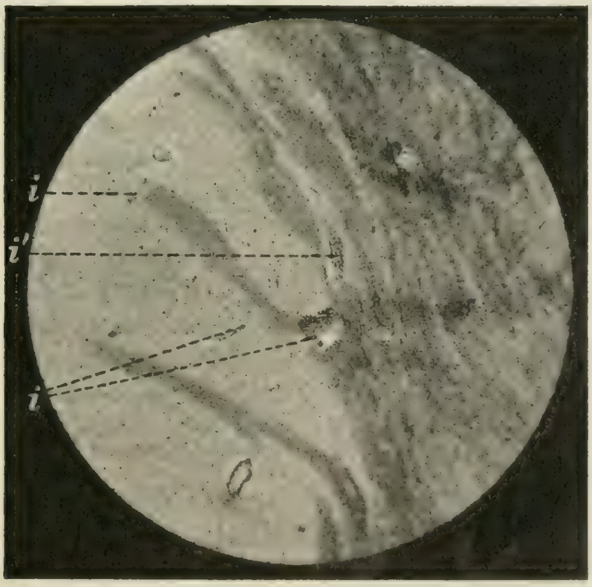

FIG 4.—Putamen and globus pallidus in a case of general paralysis. There are many patches of infiltration in the putamen (*i*) and in the lamina medullaris externæ, but none in the globus pallidus which is in the right half of the figure.

the ganglion habenulæ, the nucleus anterior thalami, the cortex cerebri and the cortex cerebelli. The deeper layers of the cerebral cortex only react clearly, the superficial stain very feebly. The cornu Ammonis often gives a stronger reaction than other parts of the cortex. Perhaps the difference in the reaction of the upper and lower layers of the cortex is connected with its differentiation into two functional regions horizontally spread over the brain, as has been demonstrated by the experiments of Nissl and Winkler, and the researches of Nieuwenhuijse, Bielschowsky, and Van't Hoog, all of which show that the lower layers are in more direct connection with other parts of the brain than are the superficial layers.

A fourth group of centres which do not react at all, or very doubtfully, includes the grey matter of the cord and medulla oblongata, the corpora geniculata, the spinal and sympathetic ganglia, and, what is very remarkable, the inferior olives despite their great resemblance in structure to the strongly reacting dentate nucleus of the cerebellum.

The centres giving the strongest reaction, as the globus pallidus, zona reticularis of the substantia nigra, nucleus ruber, corpus Luysi and nucleus dentatus, have in the fresh state a light reddish brown colour. This cannot be explained simply by the existence of iron in these centres, for Spatz has shown that the principal reaction is given by colourless iron combinations; there are centres of similar colour, as the corpora geniculata, in which iron is not found. Though it is not yet possible to explain it, the fact may be of significance.

The reaction can be also obtained in macroscopical and microscopical sections by the Berlin-blue test. This test has the advantage that the staining does not develop so rapidly, and the order of beginning and the distinction between the centres can be therefore followed more easily; but it possesses the disadvantage that the fluids themselves produce some colouration. The method is very simple: a section of the brain is placed for a quarter of an hour into a freshly made 2½ per cent. solution of ferrocyanide of potassium, and then in an abundant quantity of 1 per cent. hydrochloric acid. It is not advisable to leave the section longer than a quarter of an hour in the acid, since spontaneous staining may occur.

Fixation for one or two days in formalin does not produce marked differences, but very old formalin material cannot be used, since the formalin dissolves out the iron. Old alcohol material, however, may be employed, but the white fibres of the reacting centres, which take no colour in the fresh material, stain intensely after fixation in alcohol.

It is not strictly necessary to avoid iron or steel instruments in cutting the material.

The best method for *microscopical examination* is the Turnbull-blue reaction; it is not so satisfactory in thick macroscopical sections because it does not stain deeply enough, but in microscopical sections it gives strongly contrasting colours. The sections remain for twelve to twenty-four hours in a concentrated solution of ammonium hydrosulphide; then they are washed carefully in distilled water, and put into a mixture of 1 per cent. hydrochloric acid and a freshly made solution of 20 per cent. ferricyanide of potassium, in equal quantities; after being washed they may be stained by alum-carmin. As celloidin sections wrinkle very much under the action of ammonium hydrosulphide the celloidin should be dissolved out previously.

All these reactions render visible a part only of the iron, that in certain organic combinations, as in hæmoglobin, not reacting. In order to estimate the total quantity of iron the tissue must be destroyed and examined chemically; our histo-chemical methods show the existence of iron *in situ*, but that part of it only which reacts to these chemical tests.

In microscopical preparations the iron is seen either as: (1) A diffuse reaction of the whole tissue or of some part of it; (2) iron pigment; or (3) small granules. The latter is the most interesting form, because it proves the vital accumulation of the iron in the tissues. The granules which give the reaction have no natural colour, as may be seen in unstained preparations. They are found only in the cytoplasm of ectodermal cells (glial and nervous) of the centres of the first group, and in the putamen and the nucleus caudatus. The melanin cells of the substantia nigra contain no iron granules.

Spatz concluded that the iron demonstrable histochemically in the extra-pyramidal system has nothing to do with the destruction and synthesis of hæmoglobin; it is not increased in cases of hæmorrhages or in intravascular hæmolysis. Its quantity in the brain is very constant, in contradistinction to the liver and spleen in which hæmoglobin is destroyed and reformed.

In the fœtus and new-born child no iron is found in the brain, but the liver and spleen contain it in large amounts. It is the globus pallidus that first gives the reaction; Spatz saw it in a child nearly half a year old. The substantia nigra follows, and then the other centres, corresponding to the intensity of their reaction in the adult. It is not yet proved that the absence of the reaction in very young children is due to absence of iron in the reacting centres. It may be that in them the iron exists in a histo-chemical form in which it cannot be demonstrated by the tests employed. The brains of some mammalia give the reaction too, though not so intensely, in those portions which correspond to the areas which react most strongly in the human brain, that is the globus pallidus and the substantia nigra. Kappers employed it on the brains of birds and obtained a clear reaction in the meso- and palæo-striatum, the parts homologous to the globus pallidus. It is still more interesting that he obtained a reaction too in the nucleus rotundus, a mass of grey matter the significance of which is doubtful, though it is regarded by him as the analogue, if not the homologue, of the corpus Luysi in man which gives a distinct iron reaction.

The iron reaction gives very interesting results in the brain of patients who suffered from general paralysis. Bonfiglio [1] was the first who demonstrated that the yellow pigment found in the adventitial spaces of the vessels in this disease contains iron. Lubarsch found iron pigment without exception in more than a hundred cases of general paralysis.

The method of examination is very simple: a small piece of the cerebral cortex placed in ammonium hydrosulphide shows after some minutes characteristic dark spots and stripes in connection with the vessels, while a piece of a non-paralytic brain put into the same fluid shows only a feeble staining in the lower layers of the cortex. A small piece of the paralytic cortex, as large as a pin's head, laid on slide, rubbed with glycerine under a cover-glass and examined with the microscope, shows very characteristic deep black coloured spots along the vessels (fig. 5). This iron is hæmatogenous. Spatz found it in mesodermic granular cells, in adventitial and endothelial elements, and in Nissl's "Stäbchenzellen." These iron granules never exist in glial cells, nor in the nervous cells of the cortex.

Lubarsch found this pigment in his hundred cases of general paralysis only, and Spatz detected it in all his cases of general paralysis and in three cases of trypanosomiasis, a disease which according to Spielmeyer is closely related to general paralysis, but in no other affections of the brain. I have also found the reaction always positive in general paralysis, even in a brain which had remained for some months in formalin. As the whole test takes a few minutes only to carry out we have in it a rapid means of diagnosis of general paralysis; it may be also used as a help in the diagnosis of pieces obtained by puncture or operation on the brain.

Hallervorden and Spatz [3] have described interesting results from the application of the iron reaction to the brain of a patient with extrapyramidal motor symptoms. There was an almost exclusive affection of the globus pallidus and the substantia nigra, which in the unstained state were of a red-brown colour. The tests demonstrated here, and here only, an abundance of iron. In the majority of cases of disease of these centres, however, Spatz has not found an increase of iron.

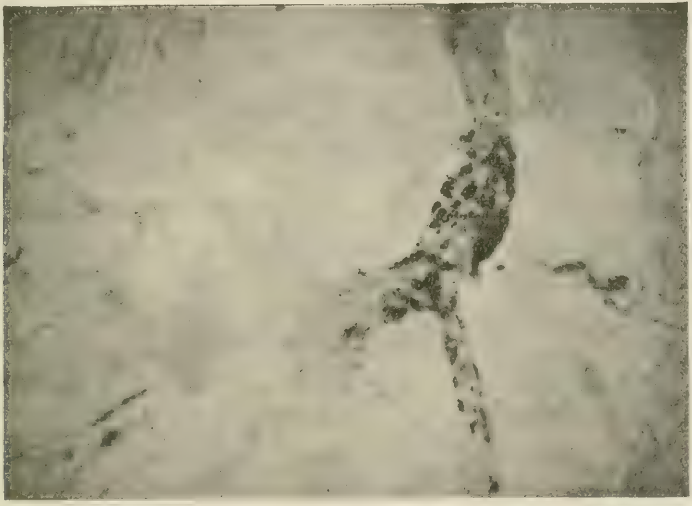

FIG. 5.—Iron reaction around a vessel in the brain of a general paralytic.

I observed in the asylum of Santpoort a young woman who suffered for some years from marked extrapyramidal motor symptoms. The globus pallidus, the putamen and nucleus caudatus were reddish-brown, especially the globus pallidus, and the iron reactions revealed a considerable increase of iron in them.

It is not my aim to give here a complete report of the results obtained by the iron reaction in the brain. I desire only to direct attention to the importance of this promising method of research, which is extremely simple and falls within the reach of every pathologist.

We do not yet know the meaning of the chemical differences demonstrated by the iron reactions, but it is of importance, especially since its investigation may lead to the discovery of other reactions which may demonstrate chemical peculiarities in centres which are the substrate of specific energies and their psychical equivalents. Theories are easily to be made, but it is a good rule, often neglected in medicine, to follow the maxim of Hughlings Jackson, that "the study of things caused must precede the study of causes of things."

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Proceedings of the Section of Neurology of the Royal Society of Medicine.

President—Dr. WILFRED HARRIS.

Meeting held December 14, 1922.

Dystrophia Myotonica.

DR. W. J. ADIE read a paper on Dystrophia Myotonica (see p. 73).

Dr. JAMES TAYLOR dealt chiefly with the familial relations of these and similar diseases. He referred to the fact that in the muscular dystrophies, Friedreich's disease, Leber's optic atrophy and other hereditary affections, there were frequently large families, especially in the affected generations; but in many of these families the mortality rate in early life is high. This seemed to him the reason why the diseases tend to die out. He also discussed the relation of the disease to the myopathies, which seemed to him to be a close one. He had seen one case of pseudo-hypotrophic myopathy in which there existed cataract similar to those found in dystrophia myotonica.

Mr. LESLIE PATON said that it was not yet possible to formulate a clear idea of the nature of the cataract which occurred in this disease. It seemed to be a posterior cortical cataract, the type found in retinitis pigmentosa and in other choroidal and retinal diseases. In a recent case he had found only a ring of granular opacities in the periphery of the lens, and peripheral striæ such as occur in senile cataract.

Sir JOHN PARSONS pointed out that the term posterior polar cataract was not an exact description; that it should be posterior cortical. This is the type of cataract which is often associated with, or results from, a general toxæmia.

Dr. WALSHE referred to a case recently under his care in which the characteristic symptoms of dystrophia myotonica were associated with other anomalous symptoms, as minor epilepsy, abductor palsy of the vocal cords, complete foot-drop, though there was very little atrophy of the muscles of the legs, and Romberg's sign. Despite the latter the sense of position and the appreciation of vibration in the legs were good.

Dr. GREENFIELD referred to the fact that in one member of the family under his care there was degeneration of the membrane of Bruch; in another case the cataract was unilateral.

Dr. HARRIS dealt with the psychical changes which are prominent in many cases of this disease, and pointed out that similar abnormalities were found in other hereditary and familial affections.

Dr. ADIE in reply said that the further study of these families brought out many interesting features. The affected families seemed to sink lower and lower in the social scale. Many dystrophic patients have had children who have been mentally defective, while others who have married have been childless. He agreed with Dr. Taylor's remarks that in the earlier generations large families were common, but the infant mortality was high. He agreed too that the term posterior polar cataract is inexact. Romberg's sign has been observed by others, as by Curschman, and in one case at least autopsy has revealed degeneration of the dorsal columns of the cord.

Meeting held March 8, 1923.

The Treatment of Neuro-Syphilis.

Dr. FARQUHAR BUZZARD said that certain principles should determine the treatment of syphilis of the nervous system. In the first place, that no distinction should be drawn between the treatment of the interstitial and parenchymatous forms of neuro-syphilis; in the second, we are justified in speaking of the cure of neuro-syphilis only when the complete eradication of the spirochæte or the continued abeyance of its activities is attained; finally, since we can never assure the patient that he is cured of the syphilitic infection, it is our duty to advise all patients who have been infected to continue intermittent treatment for the rest of their lives.

The gradual accumulation of clinical experience has shown that a negative Wassermann reaction is certainly not evidence of cure, and the fact that it has been regarded as such has made it an obstacle in the way of efficient treatment, since a negative reaction gives rise to delusions of security which often lead to the suspension of the periodic courses of treatment year after year which can alone prevent the development of neuro-syphilis or a recurrence of its symptoms. He is convinced that the view until lately held that, though meningeal and vascular lesions respond to anti-syphilitic measures, no benefit can be expected from the similar treatment of tabes and general paralysis is a mistaken one, since in both of these conditions, and especially in tabes, early diagnosis and continuous treatment are often attended by satisfactory results, though it may not be possible to abolish the symptoms of this disease already present.

The relative efficiency of various methods of treatment is still a matter of controversy. Personally, he is in the habit of using both mercury and arsenical compounds and continuing their administration periodically regardless of the results of serological laboratory tests. The only contra-indications for the use of intravenous injections of arsenic are advanced cardio-vascular changes and renal inefficiency.

Dr. HENRY MACCORMAC entered the discussion as a syphilologist rather than as a neurologist. In the study of syphilis, attention may be focused on either the signs and symptoms and the effect of treatment on them, or on the state of certain biological reactions such as the Wassermann test. These two methods are complementary, but the latter is the more important, since it is only when the biological reactions become negative that we are entitled to assume that the cure has been effective. In early syphilis it is possible not only to remove the symptoms but also to obtain a normal Wassermann reaction, but it is much more difficult to influence either the symptoms or the reactions in the later stages of the disease. He spoke of the disease being cured in its early stage when the Wassermann reaction was found to be persistently negative after a prolonged course of treatment. In the later stages the greatest benefit is obtained by a short intensive course of medication, as ten intravenous injections of salvarsan followed by twelve mercurial injections. There is an intermediate class of case in which the patients respond insufficiently to early treatment and their blood and cerebrospinal fluid give positive reactions; in these, too, there is a possibility of permanent cure by prolonged treatment.

In his opinion the existence of a neurotropic spirochæte is not yet established, and consequently there is no argument in favour of special forms of treatment in neuro-syphilis. Further, the changes found in cerebrospinal fluid in the early stages of the disease do not, in his opinion, indicate an actual involvement of the central nervous system, since the proportion of syphilitics who develop nervous manifestations is very much smaller than the proportion in whom such changes are found in the fluid. It may, however, be that in its early stage syphilis of the nervous system is curable by remedies introduced into the blood.

The treatment of neuro-syphilis is complicated by the physiological peculiarities of the cerebrospinal fluid and the difficulties of influencing it by intravenous medication, but as there is evidence that it is possible to do so in the earlier stages of infection, some beneficial effect, at least, may be expected from adequate treatment in the chronic stages of the disease. He expressed doubt as to the efficacy of spinal drainage and of intrathecal injections.

Dr. HENRY HEAD pointed out the difficulty in distinguishing, either by clinical symptoms or by laboratory methods, certain cases of cerebrospinal syphilis from general paralysis. The failure to recognize this difficulty had undoubtedly led to loose statements and very unreliable statistics, since one condition was more or less curable and the other was little if at all influenced by treatment.

Dr. RIDDOCH insisted that laboratory tests and clinical symptoms should be used in conjunction in determining the form of treatment required and its duration. In his opinion there could be no doubt that a positive Wassermann reaction indicated the activity of syphilitic processes which consequently demanded urgent treatment.

COLONEL HARRISON emphasized the fact that a negative Wassermann reaction does not mean the cure of syphilis. In his experience even general paralysis could be favourably influenced by sufficiently intensive anti-syphilitic treatment. He believed that the most important step in the prophylaxis of neuro-syphilis was the examination of the cerebrospinal fluid some time, as five years, after the original infection. He had never found fluid that was negative at this period become positive subsequently. He could not accept the hypothesis of the duality of the *Spirochæta pallida*, since all evidence at his disposal pointed to the contrary. He believed too that Dr. MacCormac was wrong in suggesting that it is chiefly on mercury that reliance should be placed in treatment in the later stages of syphilis ; it seemed to him more rational that all methods at our disposal should be adopted. He had seen some good results from intrathecal injections when the intravenous method had apparently produced very little effect.

Sir JAMES PURVES-STEWART thought it a mistake that any routine of sterotyped treatment should be adopted, as each case of neuro-syphilis demanded individual attention. It seemed to him that no drug or mode of treatment should be adopted exclusively, as each is supplementary to the others. He referred particularly to the intracisternal treatment of general paralysis. It consisted of the injection of salvarsanized serum into the cisterna magna, the beneficial action being probably due, not to the infinitesmal amount of salvarsan the injected substance contained, but to the antibodies evoked in the serum of the patient. Substances injected into the cisterna magna circulated slowly, some passing down the spinal canal, but the greater part forwards into the basilar and interpeduncular cisterns, and thence over the whole cortex, being ultimately reabsorbed by the cortical capillaries. He described the technique of the operation and pointed out that it involved very little risk. He recorded a series of cases in which under this form of treatment more or less dramatic improvement had taken place in the clinical symptoms and a fall in the number of cells in the cerebrospinal fluid, though he had to admit that he had never seen a case in which the Wassermann reaction had been made negative in general paralysis by this or any other method of treatment.

Dr. SYMONDS stated that in his experience there was very little risk in using large doses of arsenical compounds in neuro-syphilis, since they are on the whole better tolerated in these cases than by patients suffering from the primary disease. He formerly commenced by injections of 0·6 gramme of salvarsan and then proceeded to 0·9 gramme, continuing until the patient had taken 10 grammes in the first course. By this form of treatment, however, he had had several cases of jaundice and exfoliative dermatitis, and consequently he now divided the course into two, with six weeks interval between them. He also agreed that a negative Wassermann reaction might be found in both the blood and cerebrospinal fluid in progressive cases of tabes. He had at present a man under his care in whom the symptoms are increasing though the reaction is negative in both the blood and cerebrospinal fluid, but his wife's blood gives a strongly positive reaction.

Dr. FEILING spoke of the frequency of a negative Wassermann reaction in the blood and normal cerebrospinal fluid in cases of undoubted syphilis of the central nervous system. He referred to one case of syphilitic meningo-myelitis in which the Wassermann reaction was positive eight years ago but had become negative under treatment although the symptoms had progressed steadily.

Dr. HARRIS insisted that it was on the clinical rather than by biological or chemical reactions that all cases of syphilis of the nervous system should be treated. In his experience the original salvarsan or its substitute kharsivan is much more efficient than either novarsenobillon or galyl. He referred to some cases in which salvarsan had produced much improvement after these other remedies had been tried without success. He had had a considerable amount of experience in intrathecal therapy. He always waited a fortnight after an intravenous injection of salvarsan before withdrawing a patient's blood. This method had been particularly useful in tabes; though the injections generally produced intense pain for a few hours, the tabetic pains frequently disappeared for a time after each injection. He had seen no good result from intrathecal use of salvarsan in general paralysis.

Dr. BUZZARD in reply said that he could not agree with Dr. MacCormac's observations, which seemed to be mainly based on the Wassermann reaction.

In his introductory remarks he had not laid down any special routine treatment, since each patient suffering with syphilis of the nervous system required individual attention and continuous treatment, no matter what clinical form the disease assumed. He had not been convinced that the cisternal injections employed by Sir James Purves-Stewart were of any advantage, and the cases he cited did not show that it was more successful than intramuscular or intravenous injections.

Dr. MACCORMAC said that dermatitis or jaundice as a sequel to arsenical injections should be very rare, provided that this remedy was properly and intelligently employed.

NOTICES OF RECENT PUBLICATIONS.

Lehrbuch der Nervenkrankheiten. Von H. OPPENHEIM. 7te wesentlich vermehrte und verbesserte Auflage. Erster Band. S. 923, mit 323 Abbildungen im Text und 11 Tafeln. Berlin: S. Karger. 1923. Price 27 Marks.

Oppenheim's textbook has for so many years enjoyed an assured international position that the simple notice of a new edition would suffice, were it not that his death has thrown the duty of its preparation into other hands, The responsibility has fallen mainly on the late author's assistant, Cassirer, but he has happily invoked the help of Goldstein, Nonne and Pfeifer, each of whom has undertaken the revision of the subjects with which he can deal with authority.

The aim of the editors has been to alter as little as possible, and the chief changes we find are, therefore, additions made necessary by knowledge acquired during the past ten years, and especially by experiences arising from the late war.

The first volume (which is alone under notice here) has been, as compared with that of the fifth edition, increased by 230 pages, and contains 70 additional illustrations. A large part of this increase is due to a fuller description of the lesions of the peripheral nerves, and to a more complete discussion of the morbid anatomy and pathology of the diseases of the spinal cord.

The bibliographic references, which are still given in footnotes, have been kept up to date, and consequently make this edition even more useful for the purpose of reference. There can be no doubt that, under its new editors, Oppenheim's volumes will remain the most complete and reliable textbook on the subjects with which they deal.

Dementia Præcox, intermediäre psychische Schicht und Kleinhirn-Basalganglien-Stirnhirnsysteme. Von Dr. MAX LOEWY. Abhandlungen aus der Neurologie, Psychiatrie und ihren Grenzgebieten. Heft 20. Berlin: S. Karger. 1923.

In this work an attempt is made to explain the manifestations of dementia præcox on an anatomical basis.

It is assumed that there exists in man an intermediate psychic layer which corresponds with the cerebellar-basal ganglia-frontal lobe system described by

Kleist. The various centres of this system may be disturbed separately or in various combinations, both by organic lesions and in dementia præcox.

Organic lesions of the cerebellum-basal ganglia-frontal lobe system give rise to symptoms resembling those of dementia præcox, and, therefore, reasoning by analogy, it is assumed that this mental disease depends on some disturbance of this system.

The dominating characteristic of dementia præcox is described as disturbance of movement, e.g., difficulty in general movements and in movements of expression, compulsion movements, and psycho-motor reactions. Lesions of these parts have not been demonstrated in dementia præcox, and though demonstration might not be easy even if they existed, some reserve is necessary before attributing by analogy the psycho-motor alterations in dementia præcox to local changes in the basal ganglia. The multiformity of the symptoms in the disease is another difficulty, which is overcome by assuming that lesions in the various parts of the system may explain the differing syndromes, and the extent, course, direction, spread, severity and chronicity of the disease.

The similarity between some cases of dementia præcox and manic-depressive psychosis on the one hand, and hysteria on the other, is referred to; it is assumed that dementia præcox is due to disturbance of the system as a whole, while in the manic-depressive group the affective systems of the thalamus are affected, and in hysteria perhaps some parts of the basal ganglia.

There are many references to the work of Kleist, but little evidence of the existence of such an intermediate psychic layer is produced in this monograph, and no reason is offered for excluding the participation of the other parts of the nervous system in the pathology of dementia præcox. The possibility, for instance, of different compulsion movements of expression being due to psychic causes is not considered. The hope is expressed that further investigations will allow of more complete differentiation of types of mental illness in dementia præcox, but there is nothing to show how mere symptomatology and differentiation into types will lead to a better understanding of the disease.

Diseases of the Nervous System: A Textbook of Neurology and Psychiatry. By SMITH ELY JELLIFFE and WILLIAM A. WHITE. Fourth Edition, revised, re-written and enlarged. Pp. 1120, with 475 Illustrations and 23 Plates. Philadelphia and New York: Lea and Febiger. 1923. Price 9.50 dollars.

The value of such a book as this must be measured by the purpose for which it is intended or the use to which it is put. Its sub-title, "A Text-book of Neurology and Psychiatry," suggests that it is written for the ordinary student or general physician who wishes to acquire a knowledge of nervous diseases or elucidate some point of immediate difficulty, though the remarks by which it is introduced indicate that in it the authors hope to provide a handbook for the serious student of neurology. If the latter is its intended scope, the authors are certainly justified in using it as a vehicle for a "message to deliver" and in writing it around "some pervasive idea, some ideal," in other words, in presenting in it any views or hypotheses which they consider may explain the working of the nervous system and the morbid phenomena of its diseases.

If, on the other hand, the book is meant to be a guide to the student whose knowledge is rudimentary, and whose critical faculties have not been developed by practical experience with disease, hypotheses, which are merely guesses at truth and unsupported by facts and tangible arguments, should not occupy the prominent place they do in this volume. There seems, for instance, little justification for the attempt to explain so much as the authors do by primary lesions of the autonomic nervous system and disturbances of the endocrine glands ; no serious argument exists in favour of the assumption that the lesions of disseminated sclerosis may be due to the vegetative control metabolism of the spinal cord being at fault, or that myasthenia gravis is the result of a disturbance in the muscle vegetative mechanisms, or that a faulty emotional control plays a part in the pathogenesis of diabetes, or that gastric and duodenal ulcers result from increased adrenalin activities excited by the emotions of fear and hate. Such statements, unsupported by reliable clinical or experimental evidence, not only make many paragraphs of the book ridiculous, but are liable to mislead the student and do serious harm to the scientific study of medicine. In other places, as in the discussion on the mode of working of the sympathetic system, all physiological evidence is thrown overboard and is replaced by "ideas" which are more easily assimilated with the authors' creeds.

It is regrettable that these features diminish so seriously the value of a book that would be otherwise useful and fill a distinct gap. The descriptions and discussions of most diseases are clear, concise, and written with a thorough knowledge of the subjects. Diagnosis and treatment receive as a rule adequate attention, and the sections on pathology and morbid anatomy are usually sufficient for a volume of its size. Here and there there are lapses and inequalities ; the chapter on aphasia, for example, is unsatisfactory and incomplete.

The section on psychiatry is perhaps the best part of the book. The attitude of the authors to the histological lesions recently discovered in dementia præcox is interesting and on the whole commendable.

This edition has been largely re-written and carefully revised, and it consequently exceeds its predecessors in size. The illustrations, for the most part taken from other books and monographs, have been carefully chosen, and are one of the best features of the volume.

Problems in Dynamic Psychology. A Critique of Psycho-analysis and suggested Formulations. By JOHN T. MACCURDY. Pp. 377. Cambridge University Press. 1923. Price 12s. 6d.

The first half or more of this book is devoted chiefly to a destructive criticism of what the author regards as the inaccuracies and inconsistencies of Freud's doctrines. If makes dreary, barren reading. We follow the author through the maze of Freudian verbiage to come out, for the most part, nowhere. Doubtless there is much truth hidden in the Freudian hypotheses, and a constructive account from the present author of what there is of value in them to psychology would have been welcome.

The second half of the book is more interesting and readable. In it the author deals with the instincts as factors in dynamic psychology. He begins with a chapter on the late Dr. Rivers' book on "Instinct and the Unconscious," which he criticizes adversely. From this he procceds to the development of a pragmatic conception and classification of instincts, and discusses in detail the value of the ego instincts, the sex and the herd instincts, and the importance of the co-operation and conflicts of the instincts. This constructive part of the book does much to redeem the unsatisfactory, disjointed impression left by the earlier chapters.

L'Encéphalite épidémique, Étude clinique. By Louis Reys. Paris : Maloine et Fils. 1922. Price, 8.50 francs.

The study of encephalitis lethargica has recently been stimulated by the appearance of a variety of sequelæ, and a contribution to such a study from the hands of a clinician warrants attention.

After mentioning the symptoms and signs at the onset, the author passes to a detailed description of the various types of the disease to be seen in the early stages. Having devoted many pages to the disorders of the ocular apparatus, he then lays great stress on a labyrinthine type, in which giddiness, vomiting, staggering gait and inco-ordination are prominent features ; he describes several cases and claims originality for the recognition of this labyrinthine type. Reference is then made to the myoclonic and choreic types. In a contribution to the Parkinsonian syndrome he alludes to a case of this kind which rapidly developed myositis ossificans in the rigid muscles. An analysis of the effects of the disease on the sympathetic system and on the viscera and endocrine glands follows, with a suggestion that asthenic cases may result from affection in the suprarenals. The psychological aspect of the disease is briefly dismissed with a reference to the works of Truelle and G. Petit.

Following upon a few pages dealing with methods of treatment and their relative value, the author proceeds to attempt to correlate the clinical findings with the anatomy of the central nervous system, basing his views on a theoretical, at times almost hypothetical, foundation.

In discussing the late sequelæ most prominence is given to the Parkinsonian syndrome which is, in his experience, the most frequent type. He records one case which first developed signs three years after the acute attack.

Fault may be found with this volume, in that too great an attempt at classification into types is made, with the result that undue prominence is given to certain of the rarer manifestations of this disease.

[JULY, 1923.

BRAIN.

PART 2, VOL. 46.

ON HEPATO-LENTICULAR DEGENERATION, WITH THE ACCOUNT OF A CASE AND THE PATHOLOGICAL FINDINGS.

BY GEOFFREY HADFIELD, M.D.LOND.

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INTRODUCTION.

THE Danish neurologist, Hall, in a recent comprehensive monograph [1], has collected from the world's literature twenty-three cases, with autopsy reports, in which a specific organic disease of the central nervous system has existed together with a profound hepatic cirrhosis and has included a detailed study of forty-five other cases, in which, from analogy with the cases proved by autopsy, this extraordinary combination was also, in all probability, present. Previous to the publication of this monograph, cases presenting this rare, double-sided pathological picture have been diagnosed either as progressive lenticular degeneration (first recognized and described by S. A. K. Wilson), as pseudo-sclerosis (described clinically by Westphal and Strümpell, and pathologically by Altzheimer), or as torsion spasm (first described by Thomalla). Clinically, all these diseases are characterized by varying degrees of diffuse muscular rigidity, together with involuntary movements. They develop no paralysis nor sensory changes. They show a strong tendency to be familial and hereditary. Pathologically they reveal an intense hepatic cirrhosis, which in the very large majority of cases gives rise to no symptoms during life, and a varying degree of destruction of one or all of the components of the corpus striatum, together with diffuse degenerative changes of a much less severe type in many parts of the brain.

One of Hall's main theses in his monograph is that, in spite of the fact that there are many secondary points of difference in the clinical and pathological aspects of these three conditions, we are justified from their obvious general similarity in grouping them together under one term. One cannot disagree with this conclusion, which is amply justified by the rare combination common to all three diseases; and the grouping together of these three diseases is, moreover, a necessary step to take in the fuller elucidation of their unknown pathological cause, for many cases fit but awkwardly into any one of the three groups, and are, when critically examined, obviously transition types.

The case about to be described illustrates these points clearly. It will be seen that we are not justified in describing it as a clearly-cut example of Wilson's disease, or of pseudo-sclerosis, and it bore little clinical resemblance to torsion spasm. I have, therefore, described it under Hall's title of "hepato-lenticular degeneration," believing with Hall that the differences, from all points of view, between progressive lenticular degeneration of Wilson and pseudo-sclerosis of Westphal, Strümpell, and Altzheimer, are quantitative only.

A sign which appears in many of these cases is corneal pigmentation. From the published descriptions this is striking enough when specially looked for; it is due to the presence of brownish-black particles deposited in the membrane of Descemet, forming a pigmented ring about 2 mm. wide, and often only seen clearly by oblique illumination. There seems little doubt that it is found very frequently if carefully searched for. The case to be described, which was under observation for a week only, was not examined for this sign, but as we were unaware at the time of the delicacy of the pigment ring, no importance can be attached to this negative finding.

CASE REPORT.

I. U., a schoolgirl, aged 12½, was admitted to the General Hospital, Bristol, under the care of Dr. J. O. Symes, on March 11, 1922, and died on March 20, 1922.

History.—The child was normal in every respect until the age of 8. About this time she had a succession of illnesses—measles, diphtheria, and scarlet fever, and the parents state that she afterwards became delicate and needed a great deal of care. At the age of 8 she could read and write as well as other children of her age, and she had learnt to knit well. After she had recovered from these illnesses, the parents kept her from school for some time (about six months), and they noticed then that she was "rather babyish." They attributed this to the long stay at home. On returning to school she progressed very slowly. The teachers on several occasions told the mother that they "couldn't make her out," and at the age of 10 the mother found that she was "no good at anything she had to do with her hands"; for example, she had now to help her to dress, her writing deteriorated, and she could not knit as well as she could at the age of 8 years. The mother still attributing this to the child's long absence from school, says she "needed a lot of spoiling," and she found that other children were "making fun of her." From this time onwards the mother appears to have shielded and petted her in every way. She was an only child and was very sensitive of her inability to progress at school and of the awkwardness of her hands. The mother accompanied her everywhere; she ceased to play much with other children. Careful questioning regarding her general condition at this time elicited the facts that in spite of her slow progress at school the child was mentally alert, affectionate and trustworthy; she took her food well and slept well. This was her general state until a year before her death. At this time the mother noticed that often during the course of a day she had difficulty in understanding what the child said to her. She describes her speech as being "thick." At the same time she seemed to become "much more delicate" again. Her appetite became capricious, she was distressed about her school work and clung more to her mother. Very soon after this it was noticed that she had difficulty in holding things in her hands. Writing and knitting became impossible because of the "awkwardness" of her hands and she had difficulty in feeding herself. The first occasion in which this latter symptom was noticed was when late for school one morning she was attempting to eat her breakfast. The mother then noticed her hands shaking. She thought the child was nervous. The disability steadily increased. One doctor told the mother that the thick speech was due to adenoids, another, that the movements of the hands were due to chorea, and a third, that the child was "being spoiled" and was "getting too much sympathy." In spite of this, and realizing that the speech defect and awkwardness of the hands were progressing, and the child was always ailing in some respect, the mother decided to keep her at home. At this time she was in the third standard at school. She never again attended school. About May, 1921, the mother noticed that when out walking the child had developed a stoop. She scolded her for it, but says that "she stooped more and more and always held her hands up to her face." About this time the involuntary movements of the hands became very obvious, and the child developed a habit of holding her mouth slightly open, with the upper teeth "sticking out." About the time this change in facial expression was noticed the mother found that the child was always salivating. Her recollection of this is very vivid, as the child made her clothes so wet. The movements of the hands, the stoop, the altered facial expression, and the position in which the hands were held, made her extremely self-conscious if out of the house, and the mother says they came to an agreement that the child should walk behind her when they were in the streets. The child's disposition now began to change, she became irritable and restless, and had attacks of loud screaming. She developed a very marked "unsteadiness in her legs." During November, 1921, she had three attacks of copious epistaxis at intervals of a few days. All the symptoms noted above, except the epistaxis, which never occurred again, now became very obvious, and in December, 1921, she was kept in bed, chiefly because of the unsteadiness in walking. Here the greatest difficulty seemed to be in feeding herself: it was difficult for her to pick the food from the plate, she always spilled some on the floor in the attempt, and in conveying it to her mouth she lost most of it over her clothes. She was so self-conscious of her disability that she preferred to eat alone, and her mother states that "the cat had most of her food."

Most of her symptoms at this time were liable to intermissions. For a few hours at a time the movements of the hands seemed to be under control, and her speech would be fairly intelligible. When out of bed, the stoop was now extreme, and her head used to "shake in all directions." She was often noticed to make grimaces, twisting her face up, screwing up her eyes, and her mouth was often "drawn up." The mother describes a symptom, noticed first about February, 1922, which was also observed during her short stay in hospital; when out of bed she would often "dance about in the room all huddled up." From the description it appeared that in an attitude of extreme flexion she would dance in circles, lifting her feet high from the ground and "working herself up," would get very excited and often fall. During February the mother found her in the bedroom lying on the floor. She could not explain how she got there, and appeared to be "dazed." Following this she was never left alone, and on three occasions the mother says she had "convulsions," and on many occasions "choking attacks." The "convulsions" lasted about two minutes. Her arms were involved in violent tremors, her head was bent stiffly backwards, her eyes rolled from side to side, and her face "worked dreadfully." During these attacks her mouth was widely open, and she made a choking noise in her throat. On recovering she seemed to be oblivious of what had happened to her. The "choking attacks" seemed to be of the same nature, always accompanied by a marked increase in the tremor, which became almost violent, and by facial spasms. At the end of February, 1922, she had a "seizure" which lasted one and half hours; this seems to have been a prolonged attack of what the mother previously described as "convulsions." Her mother at this time described her as needing constant attention. She could do nothing for herself, and had long attacks of screaming.

Family history.—The patient was the only surviving child. A sister died in 1911 at the age of 6 years 9 months, after an illness of four months. The family doctor states that this child had ascites, an enlarged liver and heart disease. The mother is only clear on two points—that much fluid was removed from the abdomen, and that the child's face and extremities were very blue. She does not appear to have suffered from any speech defect, from difficulty in walking, or involuntary movements. Her death was certified as due to tubercular peritonitis. No post-mortem examination was performed. The maternal grandmother is still alive, the maternal grandfather was killed in an accident. The mother herself is one of eight healthy children. On the father's side, there is no history of anything suggesting that any similar case has occured in his family.

Condition on admission.—On admission the patient was found to be well-nourished, and understood all that was said to her. When undisturbed she lay quietly in bed, generally in an attitude of semi-flexion, occasionally with the lower limbs extended, and generally showing no involuntary movements. Her face was flushed, and described as being often "twisted into a vacant grin." As soon as she was approached and spoken to, all her limbs immediately became forcibly flexed and adducted. ("She shut up like a knife.") Both thighs would flex on the abdomen, and the legs at the knees. The elbows were acutely flexed and the arms adducted, the fingers being firmly clenched into the palms. The limbs were rigidly held in this position, the elbows resting on the knees; and when thus rigid, the hands and arms and the feet and legs were involved in a coarse rhythmical tremor of about four oscillations per second. The tremor was occasionally absent in the rigid legs, but always present in the arms when they were rigid. This attitude would be maintained for some minutes. It was difficult to straighten the rigid limbs and fingers, but after a time the tremor would partially cease, and the limbs could be brought to a position of semi-extension. Whilst being examined, neither rigidity nor tremor was entirely absent.

When told to move her limbs she always attempted the movement, but was generally frustrated by increased rigidity and coarse clonic movements of the limbs she was attempting to use. Simple observation, and especially any emotion, invariably accentuated the rigidity and tremor.

She had a very marked speech defect, which in common with her other symptoms was liable to intermissions, when it showed definite improvement, improving as the general muscular rigidity lessened. When she was excited or under examination her speech was limited to "yes" or "no" and short monosyllables, and her attempts to construct sentences resulted in the rapid articulation in short bursts of unintelligible sounds, with a decided nasal tone. Generally, if not harassed, she could frame short sentences of short words, but the same nasal tone was present; the words seemed to be forcibly projected one by one in rapid succession against resistance. Attempts at speech, especially if unsuccessful, increased the facial spasm, and her inability to converse caused her great distress.

Although regarded as excitable and on one occasion as hysterical, she was not very lachrymose. She cried, however, if forced against her will to perform any co-ordinated muscular movements other than walking. She attempted to obey simple commands, but generally failed if they involved any co-ordinated muscular action. The command "Turn your eyes to the right" was obeyed by a momentary flicker only of both eyes in the required direction. When told to move her rigid limbs, she generally attempted the movement slowly and laboriously, but never completed it, and showed distress and confusion at her inability to do so.

On admission her pulse rate was 136, and temperature 101° F. The temperature fell and oscillated between 98° F. and 99° F. during the nine days she was in hospital, but the frequency of the pulse (100 to 120) was maintained until her death.

No abnormality was found in the organs of the thorax. The liver dullness extended from the sixth rib to ½ in. above the costal margin in the mid-clavicular line. Neither abdominal tenderness nor free fluid was found, and no abdominal viscus was felt.

On the day of admission the urine contained a trace of albumen (0·025 per cent.). It was otherwise normal, and albuminuria was never detected again.

Nervous system.—In addition to the emotionalism, the memory was considered to be slightly impaired. There was no suggestion of drowsiness, delirium, hallucinations nor delusions, but at times she was said to be "slightly imbecilic." This was, certainly, largely due to her dysarthria.

Involuntary movements were present, as described above. They were generally most marked in the right lower limb.

There was no apparent loss of visual acuity, the corneæ were normal, but the fine pigmentation, only clearly visible by oblique illumination, recently described in this disease was not looked for. The pupils were equal and round, and their reactions normal. All external ocular movements were possible, but there was a definite inability to retain the eyes in any fixed position of conjugate deviation. There was no nystagmus. There was no loss of sensation in the skin of the head and neck. The movements of the facial muscles were equal. Auditory acuity was normal. She had some difficulty in swallowing solids, none in swallowing fluids. All movements of the sterno-mastoid, trapezius and lingual muscles were possible, but uncontrolled and jerky, and as in the limbs contraction was followed by some rigidity.

Sensory functions.—There was no complaint of pain, headache, vertigo nor tingling, and no impairment of sensation found.

Motor functions.—There was no paralysis or paresis, but a striking inability to perform any co-ordinated muscular act. She was occasionally observed to show no abnormality when lying in bed, but if she sat up or attempted to stand, her whole musculature stiffened and her limbs became involved in tremor. This happened also almost immediately she was conscious of being observed, and could never be entirely abolished whilst under examination. Her movements of general flexion ("shutting up like a knife") on being approached and during examination are described above. It was repeatedly observed that the diffuse muscular rigidity and tremor could be greatly lessened, apparently at will, but they could never be abolished while the child was sitting or standing. The intensity of both these symptoms was liable to very marked intermissions, and a definite improvement was noticed even during her tragically short stay of ten days in hospital.

Her attempts at walking varied greatly. When first admitted, attempts at walking under observation resulted in nothing more than a series of grotesque, purposeless movements. If raised from the attitude of flexion, which during her first few days in hospital she generally adopted when being examined, she seemed unable to get her feet on the floor, and had to be half carried and half supported before she could place them on the ground. Her muscular rigidity at this stage was intense, and her whole musculature involved in tremor. In an attitude of flexion, she attempted to walk by first holding to the nearest support, and then, after considerable hesitation, she would rapidly and forcibly raise one foot high from the ground and just as rapidly bring it down again. This movement was quickly followed by a similar movement of the other foot. The feet were raised apparently by a single explosive contraction of the thigh muscles, and the rigid lower limb was raised, as it were, in one piece, with the ankle-joint fixed. The result of these movements was that she succeeded in gyrating in incomplete circles about her point of support. Owing to their sudden jerky character these movements were described as being "like those of a mechanical doll propelled by strings," and the gyration as being reminiscent of a "dancing monkey." An attempt to make her walk after she had been in hospital a few days showed that she had improved considerably. The rigidity and tremor again appeared when she sat on the edge of the bed, so much so that her feet had to be forcibly placed on the ground and held there before she could get up. Her attitude on standing was less flexed and the tremor less generalized. After a latent period she suddenly and forcibly made three rapid and very uncertain short steps forwards, sprawling on completing them, and would have fallen forwards if not supported. About the same time she succeeded in reaching the lavatory, a distance of twelve yards, by pushing a chair in front of her. The arms, and often the legs during walking, were constantly tremulous, and now and then thrown into clonic contractions. It was repeatedly observed that tremor and clonic contraction were practically absent until some attempt was made to perform a co-ordinated muscular action (e.g., standing) and that rigidity was thereby increased. The hand grips were powerful and equal, but unsustained.

Reflexes.—The conjunctival, epigastric and hypogastric reflexes were present, brisk and equal. Both knee-jerks were present; they were equal and not exaggerated. The plantar reflex was flexor. The ankle, wrist and elbow jerks were brisk and equal. There was no ankle clonus. It was difficult to decide if Kernig's sign was present. There was no incontinence. There were no tropic lesions of skin or bones. The feet tended to assume a position of slight equino-varus, which could be easily corrected. It was more marked on the left side. The vertebral column was normal.

Sympathetic system.—The pupils dilated to shade and there was no proptosis, exophthalmos, nor lid retraction.

Course.—Very little change took place in her condition for four or five days after admission. Following this, a decided diminution was noticed in the tremor, and the range of voluntary movement increased.

At 1 a.m. on March 20, 1922, without any apparent premonitory symptoms, she had a series of about fifty convulsions, accompanied by violent twitching of the face and limbs. These convulsions continued almost uninterruptedly for five and three-quarter hours, she vomited incessantly, the pulse was very frequent and there was hyperpyrexia (temperature at 4 a.m. 108·2°). At first the face was flushed and red, but she gradually became cyanosed, mucus accumulated in the upper air passages, and respiration failed five and three-quarter hours after the commencement of the attacks.

Post-mortem examination (performed 7½ hours after death).—The body was that of a well-nourished child, showing no evidence of retarded development, and no abnormality externally. There was certainly no wasting of muscles and the body was well covered. The muscles were all flaccid. Nothing abnormal was found in the tongue, tonsils, or pharynx, but the larynx and trachea contained much frothy mucus. No abnormality was detected in the œsophagus. The thyroid was normal to the naked eye. No disease beyond an acute terminal pulmonary œdema was found in the contents of the thorax. There was about a pint of clear fluid in the flanks, but no adhesions or distention of the bowel. The edge of the liver was above the costal margin. No abnormality was discovered in the stomach, duodenum, small bowel, or extra-hepatic biliary system. No glandular enlargement was found. There was some congestion and thickening of the cæcum and ascending colon, but the remainder of the large bowel was normal. The mucous membrane of the cæcum was reddened, and rather velvety, and three small spherical swellings about 2 mm. in diameter, attached by broad stalks to and projecting 2 to 3 mm. above its surface, were seen in its posterior wall. Four similar nodules were found in the rather thickened and congested mucous membrane of the ascending colon. The spleen was larger than normal (weight 160 grm., long axis 14½ cm.). Its capsule was unaltered, but the pulp was firm and rather resistant, and its section was flat and appeared to be rather fibrotic. The liver showed the typical gross picture of multilobular portal cirrhosis (weight 907 grm. —32 oz.). It was shrunken and considerably deformed, its edges were blunted and its general configuration tended to be spherical. (Greatest antero-posterior diameter 8 cm., greatest diameter from superior surface to lower edge 14·5 cm.). The whole surface was studded with irregularly-sized granulations, varying from 2 to 12 mm. in diameter, yellowish or yellowish-red in colour, separated from each other by deep red, shallow depressions, and here and there by steep fissures. The capsule showed general congestion, and a moderate degree of opacity and thickening. In places this thickening was more pronounced and bridged over the deeper fissures on the surface.

On section, a wide-meshed network of fibrous tissue was seen to divide the cut surface into circular and ovoid groups of lobules, 1 to 15 mm. in diameter; these islands of lobules were light yellow, and their lobular pattern obscured. The fibrous tissue was deep red and rather

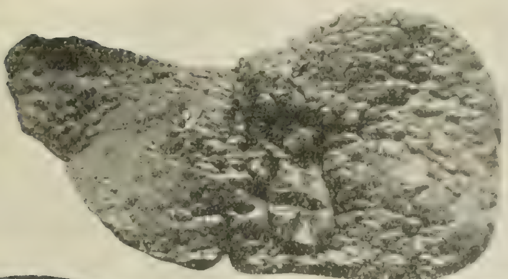

Fig I

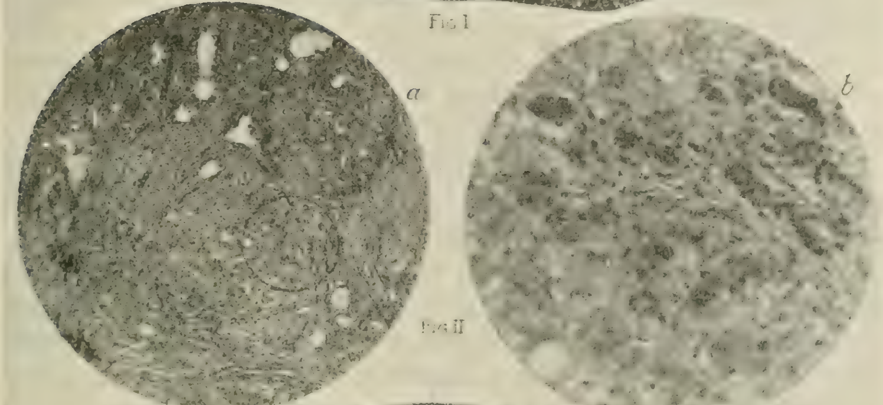

Fig II

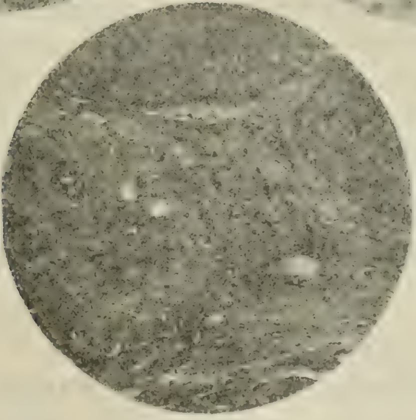

Fig III

FIG. 1.—Liver; hepato-lenticular degeneration ($\frac{1}{4}$ natural size).

FIG. 2—Photomicrographs of section of liver. *a*, Low power view showing lobule isolated by cirrhotic process. (Obj. Leitz, 3a.) *b*, Higher power view of portion included in circle in fig. 2*a*, showing proliferating bile-ducts at edge of a lobule. (Obj. Leitz, 6a.)

FIG. 3.—Photomicrograph of section of liver. Low magnification view showing broad band of cellular, vascular tissue isolating groups of lobules. (Obj. Leitz, 3a, oc. × 8.)

translucent. No changes were seen in the intrahepatic bile-ducts, or in the portal vein and its main branches.

The pancreas, kidneys, suprarenals and genital apparatus were normal.

Brain.—There were no naked-eye signs of disease in the skull, dura mater, pia-arachnoid, venous sinuses or pituitary body; middle ears were normal.

The corpus callosum was divided by an antero-posterior incision, and a horizontal section made through each cerebral hemisphere, passing through the lowest points of the splenium and genu. No obvious changes were seen in the basal ganglia or in the ventricular system. A series of coronal sections was made on each side but no gross lesion was found in the central grey matter. The mid-brain, pons, medulla, cerebellum and spinal cord appeared normal.

After the brain had been hardened in formalin it was noticed, on comparing it with the normal brain of a child of the same age, that the usual outlines of the lenticular nuclei were partially lost and their colour a deeper yellow. On cutting the frontal lobe five or six foci were found, from ¼ to ½ square cm. in area, especially about the frontal pole on each side, where the cortex looked thicker and appeared to be beset with minute cavities and dusted over with small brown dots and very delicate brown streaks. No naked-eye change was found in the rest of the brain, and this naked-eye change in the frontal cortex, in common with those in the lenticular nucleus, was only seen after careful scrutiny of the hardened brain.

The central nervous system (unfortunately partly spoiled by immediate section) was placed in 10 per cent. formol-saline, after selecting portions of the basal ganglia for alcohol and Zenker fixation, to be subsequently stained by the Nissl and Mallory neuroglia methods respectively.

PATHOLOGICAL HISTOLOGY.

Technique: Central nervous system.—Four blocks cut in coronal section were obtained of the basal ganglia from each side. At the same time similar blocks were taken from the brain of a case of lobar pneumonia, in which death was preceded by high temperature. The two series were subsequently subjected to the same methods of staining, &c. From each block two thinner blocks were cut and fixed in alcohol for Nissl staining. The other blocks were fixed in formol-saline with the rest of the central nervous system. After fixation corresponding pieces were taken from each brain and cut by the paraffin process and by freezing.

Sections were stained by the following methods :—

(1) By Goodpasture's methylene blue modification of Nissl's method.
(2) By hæmalum and eosin, and iron hæmatoxylin and van Gieson.
(3) By Lhermitte's neuroglial stain (modified).
(4) By Mallory's method for neuroglia.
(5) By scharlach R. and hæmalum.

Pieces were cut from all regions of the cerebral cortex, mid-brain, cerebellum and dentate nucleus, mid-pontine region, medulla and upper cervical cord, and treated according to the same technique. The rest of the material was put through the Kulchitsky-Pal process for myelin. Fixation of the material was considered satisfactory owing to the normal appearance of the red blood cells in all sections.

Paraffin and frozen sections were taken of several pieces of the liver and stained by methods (2) and (5) above. Paraffin sections of the cæcum, colon, mesenteric glands, spleen, pancreas and thyroid were also made.

Basal ganglia.—The corpus striatum presented very marked pathological changes, the putamen in all sections showing conspicuous diffuse degenerative disease of the bodies of its large nerve cells. No normal large nerve cells were seen in any sections, and the degeneration was of such a degree that extraneous factors, such as post-mortem autolysis and the conditions immediately preceding death, were judged to have played practically no part in its causation. After examining the series of sections cut from the putamen it was decided that, as far as its nerve cells were concerned, there was a definite selective atrophy of the large type of cell, that this process had spared many of the small nerve cells, and that degenerative changes in the small type of cell were much more recent and had not progressed as far as in the large cells. The changes seen in the large nerve cells varied. Here and there as many as ten large neuroglial nuclei, varying in form from circular to ovoid and staining weakly, were seen grouped together in a lacuna, over and under an unevenly-stained mass representing the ultimate stage of destruction of a large nerve cell, often hardly recognizable as such. This extreme change was not common, the neuronophagy usually being much less conspicuous, and the outlines of the necrotic cell distinguishable. Much more frequently were encountered very swollen cells with diffusely and irregularly stained cytoplasm, still showing indications of processes, but generally devoid of anything resembling a nucleus. Up to six pale and often irregularly shaped nuclei were present in the neighbourhood of these cells. Occasionally the nerve cell was shrunken and collapsed, and fairly frequently the cell wreck appeared to be dusted over with coarse masses and marginally-placed powdery deposits of deeply-staining irregular granules. When a nucleus was found in such a cell it was at its edge, or partially extruded, and it stained deeply and appeared deflated.

Chromatolytic changes in the small nerve cells were less constant, and the proportion affected smaller. In no case had these changes progressed to the extreme stage found in the large nerve cells, but when present they were much more advanced than those in control specimens, and such alterations as could be attributed to post-mortem autolysis and the terminal events in the disease.

FIG. 4.—Photomicrograph of normal putamen. (Stain, iron-hæmatoxylin and van Gieson. Obj. Leitz, 6a.)

The putamen showed general and unmistakable gliosis. The number of neuroglial nuclei and the type of cell both gave clear indications of this change. The increased number of glial nuclei was hardly so striking as the change from the normal in the type of cell, cells with large clear nuclei being the predominating variety. As cell destruction was so much more common in the large type of cell, the increase in the number of, and change of type in the neuroglial cells, was really the most noticeable change observed before making a detailed examination under high magnification. The nuclei of these

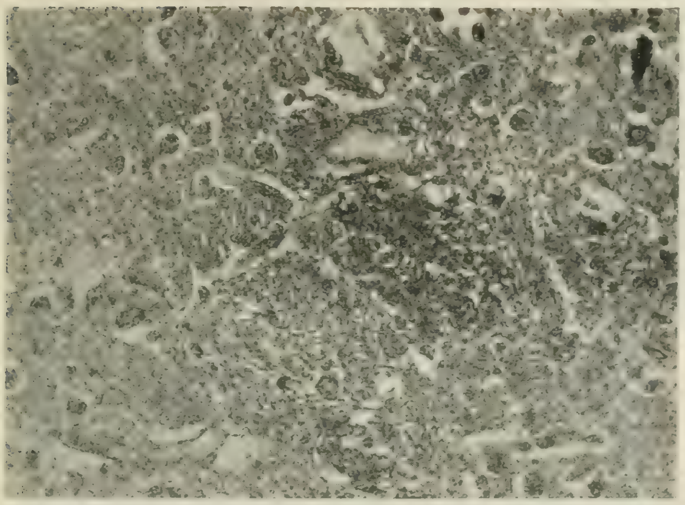

FIG. 5.—Photomicrograph of putamen in case described, under the same magnification and stained by same technique as the normal control (fig. 4). It shows increased density and sponginess of neuroglia, and many pathological glia cells.

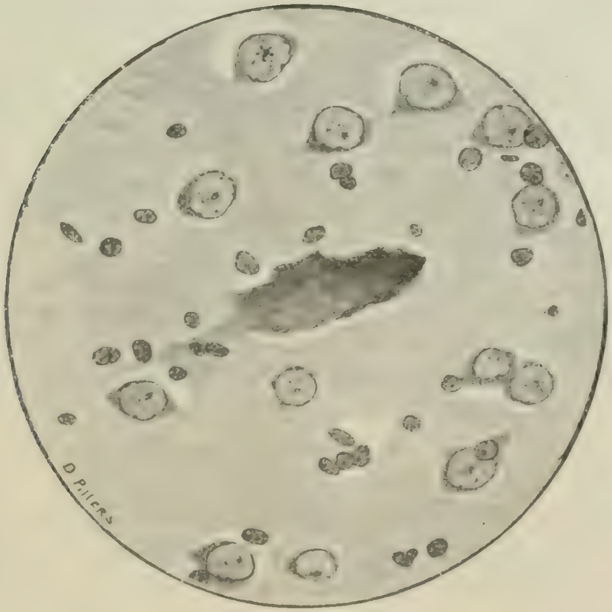

FIG. 6.—Putamen of case reported showing a necrotic nerve cell in centre of field. (Obj. Leitz, $\frac{1}{12}$a, oc. × 8.)

cells were large and clear, and stained faintly. Their shape varied from circular to bluntly spindle-shaped; some were bowed, others were slightly indented. A long search was made for the neuroglial giant cell described by Altzheimer as specific of the neurogliosis in pseudosclerosis; two doubtful examples of this type of cell were found, but in both instances it was difficult to distinguish between the neuronophagy occurring about a necrotic nerve cell, and a multinucleated cell. I experienced the difficulty, mentioned by Hall, of distinguishing between the small nerve cells of the putamen and pathological neuroglial cells, and relied chiefly on normal controls in assessing the degrees of proliferation of the latter. I could not demonstrate any neuroglial fibre formation in the putamen, and after staining many sections came to the conclusion that there was a considerable under-production of fibres by the cells, and in all probability a diffuse degenerative change in the supporting tissue, which by all connective tissue stains appeared gross, swollen and spongy-looking. No change recalling an inflammatory process, nor any disease nor alteration in the blood-vessels, were seen.

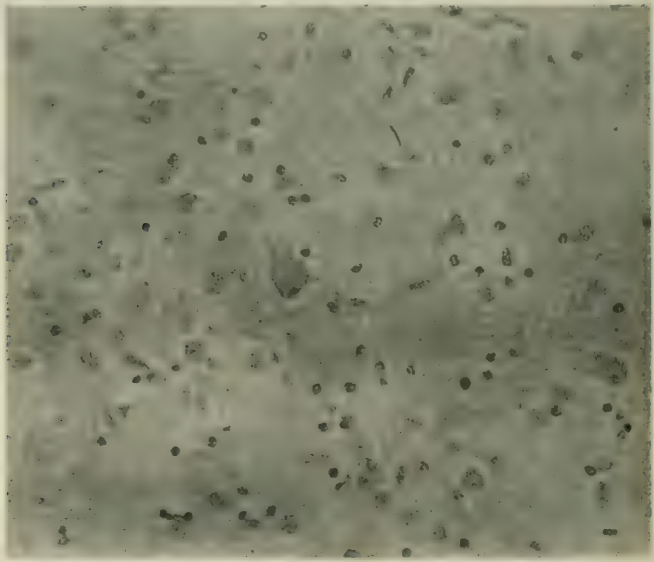

FIG. 7.—Photomicrograph of caudate nucleus in case reported. (Stained by polychrome blue, no counter-stain.) It shows large numbers of pathological glia cells, and one degenerated nerve cell in centre of field.

Caudate nucleus.—Diffuse and advanced degeneration of the bodies of the nerve cells was almost as constant in this nucleus as in the puta-

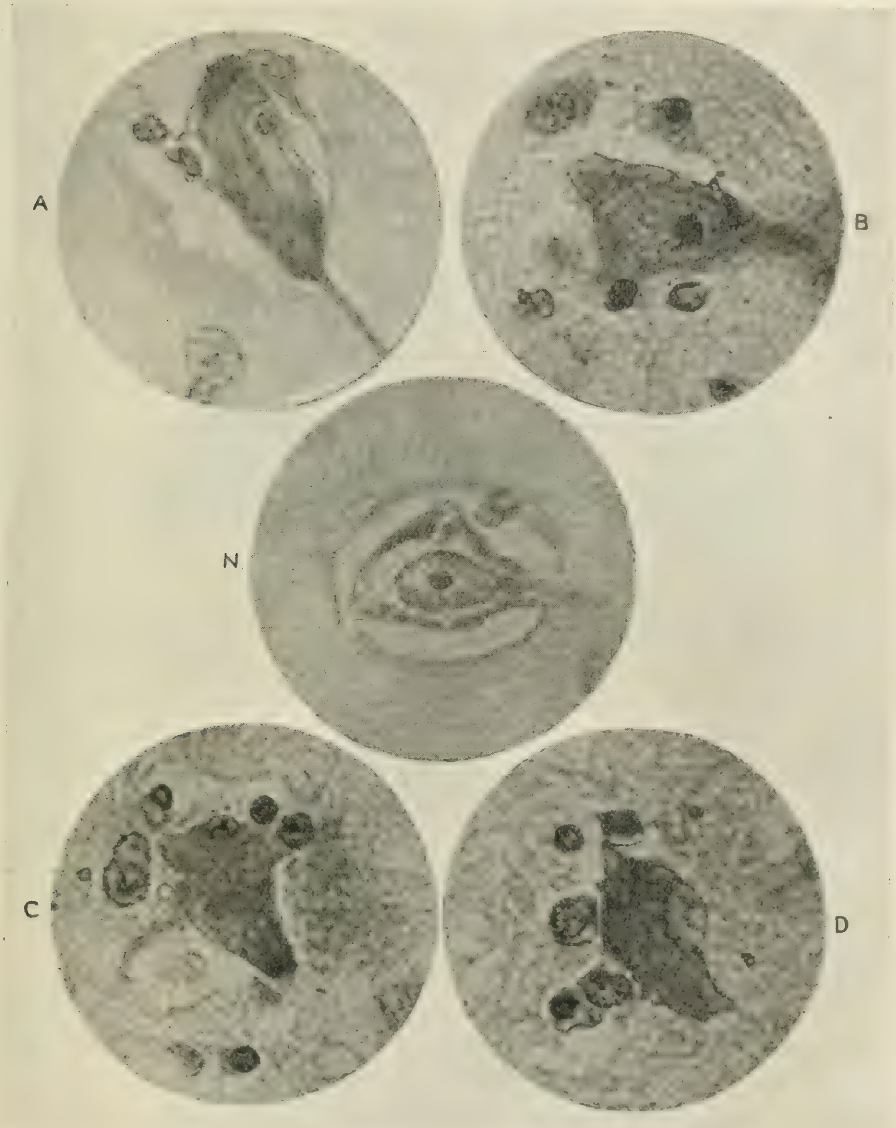

FIG. 8.—Photomicrograph of nerve cells from lenticular nucleus. (Stained by polychrome blue.) A and B from putamen; C and D from caudate nucleus; N from the putamen of a case of lobar pneumonia, dying with high temperature (normal control).

men. This was unlooked for at the outset of the investigation, but sections taken from all parts of the nucleus confirmed it. As in the putamen, the changes were diffuse, and there was no suggestion of focal lesions. On the whole, reduction of the cell bodies to shrunken masses was less noticeable than in the putamen, but the proportion of damaged cells was just as high. Neurogliosis was of the same degree as was found in the putamen. The impression left in one's mind after examining both nuclei was that the lesion in the putamen was somewhat older. In both the putamen and caudate nucleus, frozen sections did not show more than a few scattered granule cells staining by scharlach R., and the Virchow-Robin spaces were practically free of cells of this type.

Globus pallidus.—The nerve cells of both segments were singularly free from the extreme changes found in the caudate nucleus and putamen, but degenerative changes in the bodies of the large motor cells were generalized and diffuse. The commonest change consisted of swelling of the cell with excentricity of its nucleus, powdery marginally placed Nissl granules, and diffuse staining of the cytoplasm. Neurogliosis was not so marked as in the putamen. The change was obvious in most fields when examining this nucleus with a low power, but occasionally two or three fields would be encountered which demanded fairly critical comparison with normal controls to establish any alteration. The neurogliosis was of the same type as was found in the putamen.

Optic thalamus.—An occasional cell was found in sections showing slight degenerative changes, but hardly of a greater degree than would be accounted for by the mode of death. There was no definite neurogliosis.

No constant clearly-cut lesions were found in sections of the subthalamic nuclei, mesencephalic nuclei, or in the grey matter of the pons and medulla oblongata.

Cerebral cortex.—The small naked-eye foci showing increased thickness and a finely pitted appearance in the cerebral cortex of the frontal lobes in the formalin-hardened brain were very obvious under low magnification in stained specimens. All the pieces showing this change, selected from the frontal region, were difficult to prepare by the paraffin and freezing methods because of their increased friability. Under low powers these regions of the cortex showed a uniform gross abnormality, consisting of a prolific new-formation of well-developed blood-vessels occupying fairly accurately the area of cortex extending from the middle of the supraradiary layer to the junction of the grey and white matter.

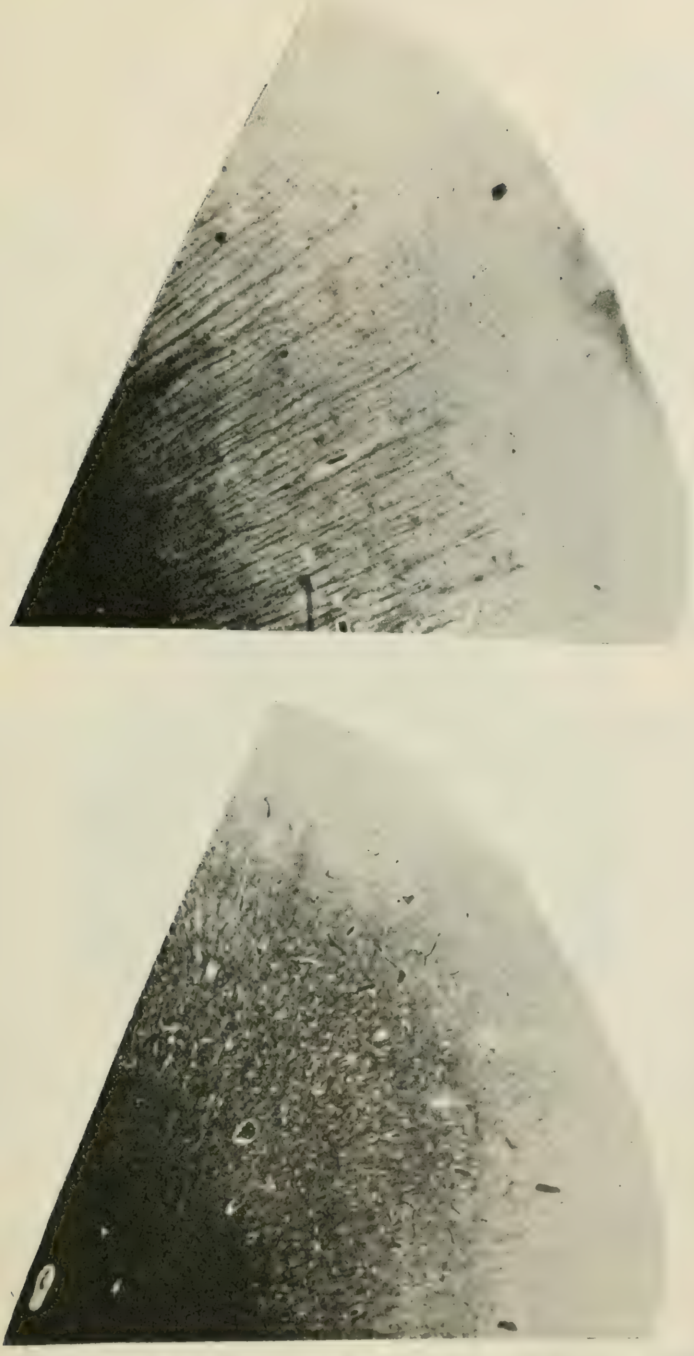

FIG. 9.—Photomicrograph of section of superior frontal gyrus. (Stained by Kultchitsky-Pal process.) The upper photograph was taken from the edge of a focus and is almost normal in appearance, the lower from a focus of vascular new formation.

In the radiary layer this vascular new formation was sufficiently developed to cause very considerable distortion, interruption and degeneration of the nerve fibre bundles of this layer, and to obscure the cyto-architecture to a marked degree. It was to this new formation that the naked-eye pitting and friability of sections of this part of the cortex were due. The small cavities were probably only exaggerations of the normal perivascular spaces around the larger of the newly-formed vessels.

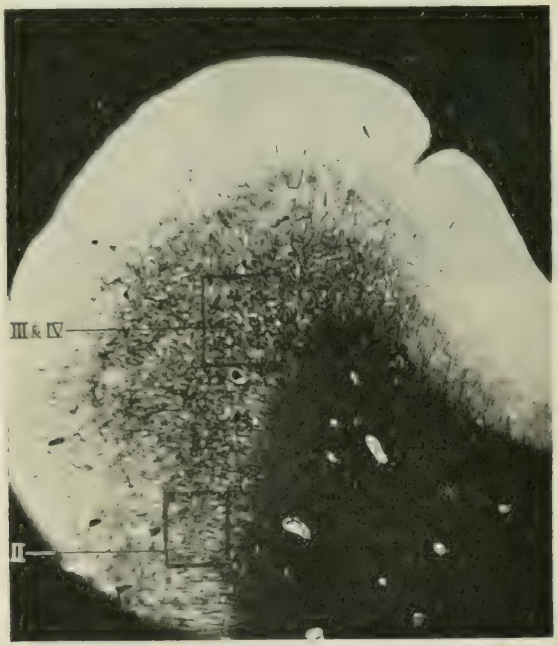

FIG. 10.—Photomicrograph of a vertical section of the cortex of a frontal convolution. (Stained by the Kultchitsky-Pal process. Magnification × 14.) It shows a focus of vascular new-formation occupying the free surface of the convolution. The areas enclosed in numbered squares are represented under higher magnification in next figure.

The same change was found but to a much less extent in many parts of the cortex; the degree shown in figs. 9 and 10 existed only in the frontal cortex of both sides, especially in the anterior part about the frontal poles and in the anterior halves of the superior frontal gyri. Here the vessels were very tortuous and in thicker sections formed spirals, closed loops and knots often causing complete interruption of the larger nerve fibre bundles. There was no indication that the vascular new-formation was derived from the pia-arachnoid. It was accompanied by no inflammatory changes, and the walls of the vessels were so well formed and the vessels themselves appeared to be so well accommodated in the tissue that congestion and dilation of previously existing vessels could be definitely ruled out as a cause of the condition. The vessels were for the most part of the calibre of capillaries and pre-capillaries; most of the latter had a delicate well-formed elastic lamina and a single or double layer of muscle-cells. Some vessels of the calibre of pre-capillaries contained no elastic tissue in their walls, and in a considerable

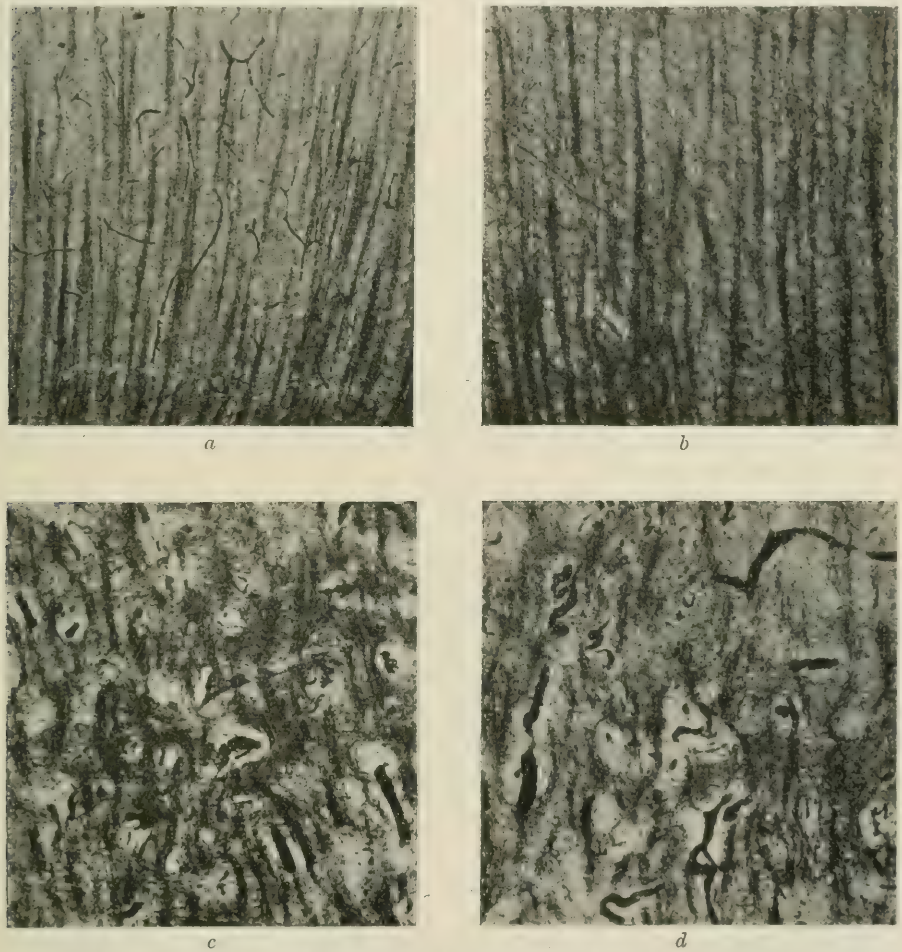

FIG. 11.—*a*, Normal control; Weigert-Pal preparation of the frontal cortex of a normal brain, but showing prominent vessels. *b*, Cortex included in area marked II in fig. 10, taken from the edge of the lesion. *c* and *d*, Cortex included in area marked III and IV in fig. 10, showing new-formation of vessels and interruption of the bundles of nerve fibres.

number of these the lumen was very considerably reduced by thickening, corrugation and infolding of the vessel-wall. In some the thickening of the wall was due to hyperplasia of muscle-cells, but in the majority it appeared to be a result of a rich investment of the wall by a closely-set and abnormally rich neuroglial network (see fig. 12, *a*). In no sections were the vessels dilated ; the majority contained blood-cells, and no thrombosis was seen. The perivascular spaces around the vessels were large and roomy. It was exceptional for any vessel to fill its space completely, which was generally empty except for two or three "granule cells" containing lipoid granules. The abnormally roomy perivascular spaces were almost as prominent in frozen as in paraffin sections, and, owing to the tortuosity and frequent branching of the vessels they contained, a general view under low magnification gave the impression of many branching linear cavities containing central vessels, lying at all angles to each other, and separated by diffusely and deeply stained, yet richly cellular supporting tissue. There was no evidence that the cavitation was due to any other factor than this, for although the parenchyma was considerably altered it showed no gross softening nor intrinsic cavitation.

The vascular new-formation spread for a short distance only into the white matter, and was generally most intense at the summit of the convolution, the cortex lining the floor being often quite free from the change. It was peculiarly localized, the free surface of one convolution would show the change over an area not exceeding one square centimetre, the neighbouring one would show the same change over a similiarly sized area, but at a distance of 3 or 4 cm. away. These lesions were bilateral and most marked in the frontal lobes, being present on their superior, anterior, and antero-inferior surfaces ; they were not, however, rigidly symmetrical, the foci on each side being scattered apparently at random over the surface. The extreme change in the frontal lobes apparent on naked-eye examination in the formalin-hardened brain was not visible elsewhere, but in sections taken from other regions a milder degree of the same changes was fairly frequently seen. In no case was this sufficient to cause the same gross nerve-fibre degeneration nor deformity of the cell-layers.

Where the affection was most marked, the supporting and nervous tissue showed striking changes. The neuroglia in its staining reactions was very similar to that found in the putamen—coarse, diffusely-staining and cellular. It contained a moderate number of the same large fibre-free glial cells as were found in the putamen,

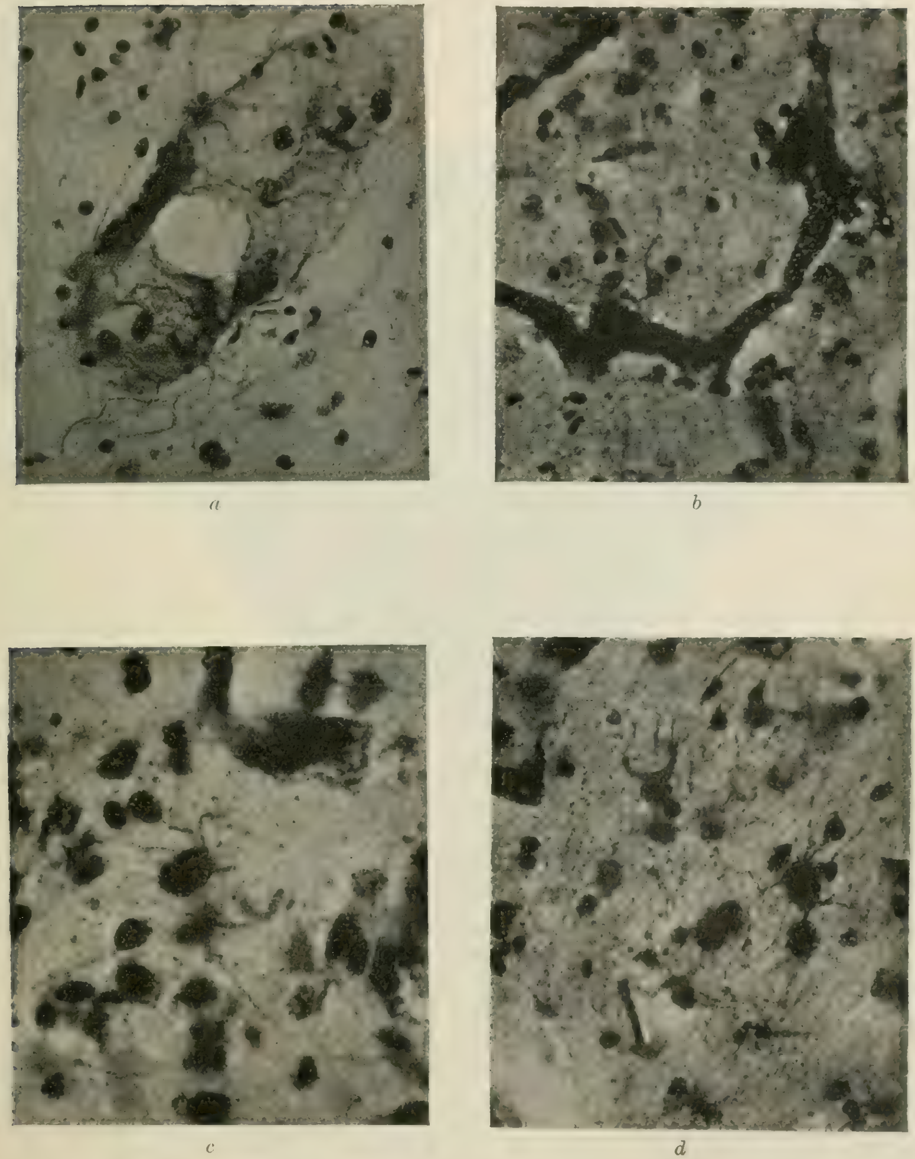

FIG. 12.—Photomicrographs of sections of the frontal cortex through a lesion similar to that shown in figs. 9 and 10, stained by Lhermitte's method for neuroglial fibres. *a* Shows neuroglial investment of the wall of a newly-formed vessel; *b* shows spider-cells in close relation with the wall of the vessel; *c* and *d* show large type of fibre-forming glia cells found in large numbers in the cortical foci.

but there were in addition considerable numbers of large fibre-forming glial cells, especially where the vessels were most numerous. (See fig. 12, *b*, *c* and *d*.) The same difficulty was found in distinguishing large glial cells from small nerve cells, but by comparison with normal controls it appeared certain that the cell increase in these cortical foci was due to the presence of pathological neuroglia.

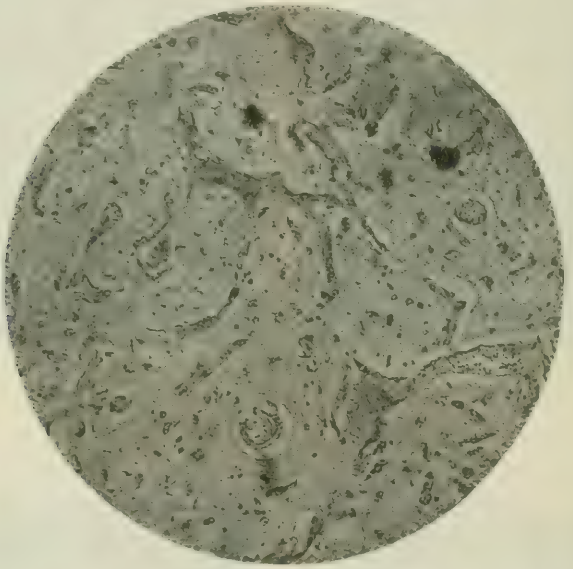

FIG. 13.—Photomicrograph of section of a cortical focus similar to that shown in figs. 9 and 10. Note the new formation of vessels. (Obj. Leitz, 3a, oc. × 8.)

Degeneration of the cortical cells was confined to the areas where the vascular new-formation was present. Here it was considerable and had affected an appreciable number of the medium and large pyramidal cells. Much of this cell degeneration must be ascribed to the distortion and degeneration of the fibre bundles, caused by the prolific vascular new-formation, since the Weigert-Pal preparations showed a marked degree of fibre degeneration. In both layers of large pyramidal cells all the extreme grades of degeneration were present and satellitosis was established. Loss of nucleus, shrinking and diffuse deep staining of the cell-body were the commonest changes. There was no doubt, however, that compared with the cell degeneration in the striate body the process was much less uniform, and some pyramidal cells, especially at the edge of the cortical foci, had escaped, whilst a considerable number of the small pyramidal cells were intact.

Cerebellum.—No definite lesions were found in the cerebellar cortex. The majority of the cells of the dentate nuclei presented degenerative changes consisting of shrinking and atrophy of the cell-body and deep staining of the cytoplasm. There was mild neurogliosis in the nuclei, but no gross lesion such as was found in the putamen of the lenticular nucleus.

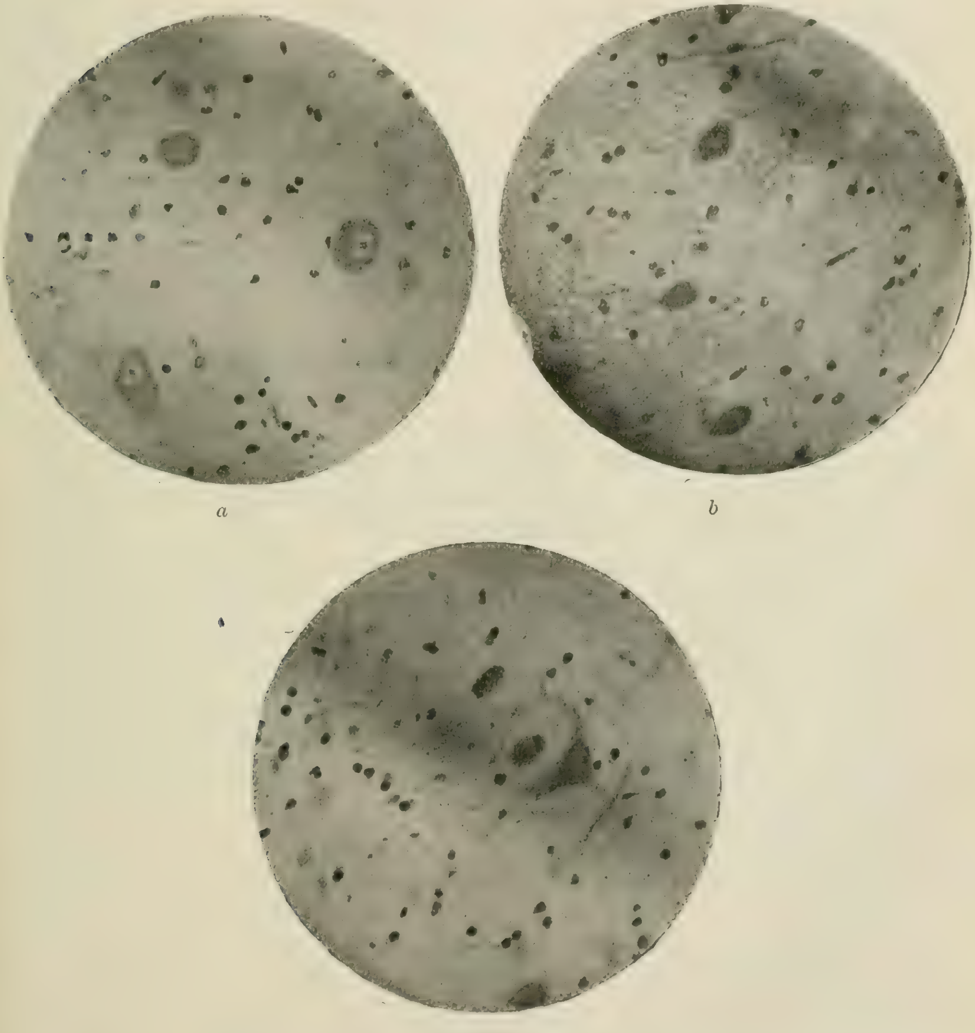

FIG. 14.—*a*, Photomicrograph of a normal dentate nucleus, stained by polychrome blue; *b* and *c*, dentate nucleus in case reported, showing two groups of degenerated nerve-cells. (Technique and magnification as in the normal control.)

Subthalamic fibre system.—Many factors contributed to make this examination unsatisfactory, the chief being the fact that at the autopsy this region was cut in many places, making it impossible to orientate the pieces afterwards. However, a few sections were obtained which showed definite and well-marked degeneration of the fibres of the ansa lenticularis. The change was gross and shown well by the Weigert-Pal method. Dr. Blachford, of the Bristol Mental Hospital, gave me considerable help in the anatomical localization of the degeneration, and expressed complete agreement with this diagnosis.

Liver.—The naked-eye appearances of multilobular cirrhosis were confirmed microscopically. A wide-meshed network of fibrous tissue was seen to enclose in its meshes groups of three to eight liver lobules. This cirrhotic process had the following salient characters:—

(*a*) It was excessively vascular.

(*b*) It showed no tendency to invade the isolated lobules except at their extreme edges.

(*c*) It was composed of broad sheets of rather immature fibrous tissue, lying in which were: (1) A prolific new-formation of bile capillaries, and (2) many foci of mononuclear cells tending to be disposed in relation to the walls of the numerous vessels.

The liver cells of those lobules in the centre of the isolated groups of lobules were normal, except for recent venous congestion, and little change was found in the more peripheral lobules, except towards their edges. Here the fibrosis had cut off and isolated groups and columns of liver cells, and very occasionally had completely isolated a lobule. The cells of these isolated lobules and groups showed all pathological changes from moderate fatty infiltration (with single droplets and an eccentric normal nucleus) to the changes associated with cell-death.

As the number of isolated single lobules was small, and the isolation of cell groups not conspicuous, the amount of actual destruction of the hepatic parenchyma was not large. The increased vascularity of the fibrous tissue was due to the presence of enormous numbers of widely-open, thin-walled fragile vessels, which were confined to this tissue, and, like it, showed no invasion of, nor connection with the hepatic lobules. They were generally lined by a double layer of endothelium, were devoid of an elastic lamina, and the muscle was either absent or very scanty. The fibrous tissue itself was obscured by them, but it appeared to be much more mature and of older date, especially at the edges of the lobules. Toward the centre of the cirrhotic bands it was less mature. The bile capillaries were numerous, and their epithelium actively growing. They showed little tendency to invade the lobules, or to fuse with the more or less isolated liver cells lying in the cirrhotic tissue. No bile stasis was seen in them.

The collections of mononuclear cells appeared to lie in foci within the fibrous tissue. In some parts they were few, in others a rich infiltration of the tissue was present. They were constantly most numerous around the thin-walled vessels, and immediately surrounding the vessels a fairly high percentage of them were polynuclear. Others were typical plasma cells, and at the edges of these cell collections the majority were typical lymphocytes.

Sections of the liver stained by Gram's method showed no organisms, and no result was obtained in sections stained for pathological pigmentation.

Colon.—Cultures were made from the cæcum, the transverse colon, the descending colon and the mucous membrane of the ascending colon. No pathogenic organisms were isolated.

The nodules in the cæcal wall consisted of polypoid projections of hyperæmic inflamed mucous membrane, overlying a somewhat fibrotic submucosa. There was no gross loss of mucous membrane in any section, but the glands in all sections were widely separated by an abnormally rich cell-exudate. This was true of all sections taken of the mucous membrane, as far as the splenic flexure, but it was most noticeable in the cæcum. Here and there were microscopic patches in the mucosa devoid of gland tissue, which was replaced by hyperæmic cellular tissue, in which a few groups of epithelial cells, the remains of gland-tubules, lay. The cells were chiefly of the large mononuclear type, lymphocytes were not conspicuous, but polymorphonuclears were fairly numerous. These microscopic gaps in the mucous membrane were numerous, and, taken together, represented a considerable loss of surface.

Although hyperæmia was prominent in these foci, no constant perivascular arrangement of the cell-exudate nor thrombosis of vessels was seen, and the fixed connective tissue reaction was not marked. Below these small breaches of surface, the muscularis mucosæ was pierced by the cell-exudate, but this did not extend far into the submucous coat which, on the whole, together with the other coats of the bowel wall, appeared normal. The lesion was regarded as a widespread subacute catarrhal colitis.

SUMMARY OF CASE.

A girl, aged 12½ years at the time of her death, was noticed at the age of 10 to be awkward with her hands in writing and knitting, having been previous to this in all respects a normal child. This disability progressed slowly, and her speech became indistinct. She developed a stoop, a change in facial expression, excessive salivation, and a gross speech defect. Her motor disability progressed, and she developed coarse tremor of both upper limbs. At the age of 12 she could hardly walk, strangers could not understand her speech, and the tremor of the hands made it difficult for her to feed herself. During the last six months of her life all her symptoms became rapidly worse. She developed intermittent facial spasms, a gross speech defect, and a diffuse rigidity of her voluntary musculature, which made walking, sitting and standing almost impossible. These symptoms varied in intensity and she became subject to convulsions. She died two and half years following the onset of the disease, after a series of epileptiform convulsions lasting several hours.

Clinical examination revealed a diffuse muscular rigidity, affecting agonists and antagonists equally, which was increased by any attempt at co-ordinate muscular contraction and by emotion, but subject to intermissions during which its intensity lessened considerably. Associated with the rigidity, and increasing and decreasing with it in intensity, there was a coarse tremor of all four limbs. Attempts at walking resulted in a series of grotesque, disordered movements, in which she contracted all her muscles, but failed to accomplish the act. She had a marked degree of dysarthria. She was not paralysed, and had no sensory changes.

On post-mortem examination she was found to have an intense multilobular hepatic cirrhosis. The central nervous system showed no naked-eye changes, but microscopically the lenticular nucleus presented widespread degeneration of its nerve cells, and replacement of its supporting tissue by neuroglial cells of a pathological type which formed no fibres. This change was bilateral, and of equal intensity on the two sides. There were degenerative changes in the ansa lenticularis. The cortex of the frontal lobes showed foci just visible to the naked eye, in which a prolific vascular new-formation, nerve-fibre degeneration, and a considerable degree of nerve cell destruction were present. The nerve cells of the dentate nuclei were degenerated.

DISCUSSION.

The case reported bears a strong clinical resemblance to Wilson's disease, showing most of its essential positive features; yet the pathological examination, especially the striking absence of naked-eye changes in the brain, is in favour of classifying the case as one of pseudo-sclerosis. This is brought out clearly by tabulating the main characters of the two classical types with those common to both, and comparing them with those found in the case described. In this way it becomes obvious that the case described does not fit accurately into the progressive lenticular degeneration group, nor into that of pseudo-sclerosis. For many of the facts in the following table I am indebted to Hall's painstaking analysis of the published cases, and where figures are mentioned under the heading, "Hepato-Lenticular Degeneration," they are his.

There seems little doubt that practically all the symptoms, and certainly all the motor disabilities found in the diseases comprised under the term "Hepato-Lenticular Degeneration," are due to the diffuse generalized muscular rigidity invariably associated with them. In the case reported, this rigidity was well established and had produced an extreme degree of dysarthria, but it was apparently not so intense as in the classical types of progressive lenticular degeneration; it had not reached the stage where the whole voluntary musculature is permanently rigid during the waking hours; no muscular contractures were present, and a very marked diminution in the rigidity could be obtained if the muscles were put at rest. The patient enjoyed intermissions when at rest, during which the rigidity and its resulting symptoms almost disappeared. In spite of this, the positive nature of the symptoms was certainly of the order found in Wilson's disease, with which is invariably associated a naked-eye destructive lesion of the lenticular nuclei. The pathological examination, however, failed to show any gross change in the brain, and we are forced to look closer into the histological changes found in this case to explain the contradiction.

In pseudo-sclerosis the muscular rigidity and the destructive changes in the lenticular nucleus are minimal; in progressive lenticular degeneration the rigidity is intense and the destruction of the putamina often total. The histological changes in the case described consisted of a pathological neurogliosis which had entirely replaced the normal glial tissue of the putamina and caudate nuclei, and a selective necrosis of the large nerve cells of these nuclei. This change was sufficient to give rise to all the positive signs of Wilson's disease. It appears likely, therefore, that

	All cases grouped together as hepato-lenticular degeneration	Progressive lenticular degeneration	Pseudo-sclerosis	Case reported
Age at onset .. Greatest incidence	Between 11 and 25 .. .. Limits : 3 to 41 years ..	Between 15 and 20.. .. Tends to include the younger patients	This type generally in patients in which the onset is between 30 and 45	10 years
Sex	Males predominate : 50 males to 18 females. (Hall)	Sexes appear to be more equally affected	Males predominate	Female
Duration (when disease itself caused death)	2 to 7 years (average) .. Limits— 1 month to 11 years. (Hall)	2 to 7 years (average) .. Limits— 4 months to 7 years (Wilson)	As Wilson's disease	2½ years
Family history ..	Is familial, and in one generation in half the cases. In two cases has appeared in several generations. (Hall)	Equally marked familial tendency	As Wilson's disease	No family history obtained
Motor system— (1) Muscular rigidity	Always present and generalized : degree of rigidity varies ; is not pyramidal ; affects agonists and antagonists equally	Is always a marked feature ; dominates the clinical picture ; may terminate in contracture attitudes	Much less intense ; may escape notice, but often obvious and probably always present	Generalized and intense in movement and standing ; marked relaxation during intermissions ; always very variable
(2) Involuntary movements	Generalized tremor the most common Always increased by voluntary muscular contraction	A salient feature .. .. Increases as disease progresses; the muscular rigidity tends to mask it	Always present, occasionally very marked ; is a striking feature	Always present in voluntary muscular contractions, but not a striking feature otherwise ; of the same type as in preceding
Reflexes..	Not altered .. .. .. Abdominal reflex present ..	Normal, but difficult to elicit when rigidity is intense Abdominal reflexes present	As in Wilson's disease	As in Wilson's disease
Walking	Difficulty in walking present in all cases, but varies within wide limits	Great difficulty always ; progresses to complete inability to walk or stand	Often only moderate difficulty ; rarely so marked as in Wilson's disease	Great difficulty even in standing, walking almost impossible
Facial aspect	Every gradation from facial immobility (of Parkinsonian type) to intense facial spasm	Intense rigidity of facial muscles. Widely-open eyes and mouth. Powerful facial spasms. Tongue muscles rigid	Spasm and rigidity inconspicuous. Immobility and mask-like expression generally	Moderate rigidity only. Mouth not held widely open. Rigidity well marked during attacks of spasm. Face always flushed

	positions (e.g., of tetany), with arms adducted ; every gradation between this and slight general rigidity			under observation. Subject to marked remissions
Speech defect	Varies from slight dysarthria to complete anarthria ; always slow and spasmodic ; relaxes with the muscular rigidity which causes it	Always present, marked and progressive, reaching complete anarthia. No paralysis or atrophy of muscles concerned	May be a quite slight defect only. Generally present, but to a considerably less degree than in Wilson's disease	Was a striking feature. Speech limited to a few monosyllables
Difficulty in swallowing	Variable, depending on degree of rigidity. Fluids generally easily swallowed	Generally a very marked difficulty	Usually only slight dysphagia	Not a marked feature
Corneal pigmentation	Present in more than half the recorded cases	Has been described in typical cases	Very commonly present ..	Was not specially looked for
Mental state	A varying degree of dementia. Generally slight	Dementia not marked	Tend to show more marked mental change	Not demented. Some diminution of intellectual powers
Abdominal organs ..	Generally no abdominal symptoms. Liver dullness generally diminished	No clinical signs, and only vague symptoms	As in Wilson's disease	Attacks of epistaxis. No other signs
Pathological changes in central nervous system	Nerve-cell destruction and neuroglial proliferation most marked in the corpus striatum but often diffuse, yet of less severe degree, throughout most of the brain. Dentate nucleus and cerebral cortex often involved. Changes vary from gross naked-eye cavitation to discoloration of lenticular nuclei, down to absence of any naked-eye changes	Characterized by naked-eye changes, and a sharply demarcated lesion, viz., bilateral, symmetrical softening of the lenticular nucleus, with cavitation of the putamen. This change is present in all clearly cut cases of Wilson's disease. Degeneration of tracts connecting striate body to thalamus, subthalamic body and red nucleus. Economo describes cortico-striate degeneration. A diffuse neurogliosis has been found since Wilson's publication, similar in all respects to that of pseudosclerosis. Occasionally cavitation has been described in the cerebral cortex	No naked-eye changes as a rule, but diffuse degeneration throughout brain. Yet this chiefly in basal ganglia, and especially in lenticular nucleus. The hypothalamus, cortex cerebri and dentate nucleus are often involved. Change is a degeneration and destruction of nerve cells, with marked progressive neurogliosis. Altzheimer describes as occurring frequently in all parts of C.N.S., a neuroglial giant cell. Universal distribution of this cell not confirmed since his description. All observers agree that a diffuse neurogliosis, characterized by large numbers of neuroglial cells with large pale nuclei, is present. This usually found in grey matter only. Hall finds it in the white matter also	No naked-eye changes. Diffuse uniform degeneration of large nerve cells of putamen and caudate nucleus of corpus striatum, with degeneration of its fibre system and marked neurogliosis. Degeneration of fibre system and a prolific vascular new formation in several foci in the cortex, specially in the frontal lobes. Cell degeneration in these foci of cerebral cortex, and in dentate nucleus, but to less degree than in putamen and caudate nucleus. Altzheimer cells not numerous. Wider diffusion of changes throughout the central nervous system not found

	All cases grouped together as hepato-lenticular degeneration	Progressive lenticular degeneration	Pseudo-sclerosis	Case reported
Liver	Gross multilobular cirrhosis with reduction in size of liver always present, and practically always symptomless. Nodules larger than in Laennec's cirrhosis. This probably explained by the youth of the patients (Hall) Histological characters : — (*a*) Very cellular, broad cirrhotic tracts, containing large numbers of proliferating bile ducts. (*b*) Isolated lobules and cirrhotic tracts always very vascular. Vessels are branches of portal vein. (Kleiber and Hall) (*c*) In a few cases foci of necrosis and lobular destruction described	No constant difference noticed in either disease in this respect		Focal necrosis not found

the histological changes described in the lenticular nuclei in the case reported, represent a stage in its functional destruction not far removed from the total degeneration found in well-established cases of Wilson's disease.

As regards the changes found in the other parts of the brain, the small foci of degeneration and vascular new-formation in the cerebral cortex were as striking as they were unexpected. A similar change has been found in the corpus striatum in this disease by Pollock and by Spielmeyer. Pollock found in silver-impregnated preparations of the lenticular nucleus in this disease a dense network of thickened vessels ramifying irregularly and pervading the whole of the putamen. In sections stained by hæmatoxylin and eosin this appearance was not found. Pollock insists that this appearance is only obtained by impregnation methods. Hall found a similar vascular proliferation in the dentate nucleus and red nucleus. He is inclined to regard the change described by Pollack as due to atrophy and retraction of the wasted nucleus. Spielmeyer found a striking proliferation of vessels and of perivascular connective tissue in the most degenerate parts of the corpus striatum. He discovered a similar change in the dentate nucleus, but in neither nucleus any accompanying inflammatory changes. Spielmeyer also found focal lesions in the cerebral cortex of the occipital lobes, in which the changes were of the same type as those found in the lenticular nucleus, i.e., intense nerve-cell degeneration and marked neurogliosis. Howard and Royce have described, in a case having a duration of one month (the most acute case published), cavitation in the caudate nucleus, optic thalamus and red nucleus, similar to that found in the putamen.

It is probable, therefore, that the changes in the cerebral cortex are of the same nature as those found in the lenticular nucleus, but of more recent origin or of a less acute type. I am not inclined to agree with Hall that the vascular new formation is probably due to wasting and retraction of the grey matter. The change described in my case was quite unlike that found in an organ undergoing atrophy, and its intensity was out of all proportion to the amount of wasting. It seems probable that this change is an early stage in the same pathological process which eventually ends in nuclear destruction, and that it appears in extra-lenticular foci, because they are affected later.

It is my pleasant duty, in conclusion, to thank Dr. J. Odery Symes, Physician to the General Hospital, Bristol, for permission to publish the case, for the use of his clinical records and encouragement in the investigation.

I am considerably indebted to Dr. J. V. Blachford, the Superintendent of the Bristol Mental Hospital, for placing at my disposal his intimate knowledge of the anatomy of the nervous system, and for kindly criticism and advice in the preparation of the paper and examination of the material.

CONCLUSIONS.

(1) A case is described having all the essential characters of hepato-lenticular degeneration.

(2) It illustrates conclusively, both clinically and pathologically, the existence of transition types between Wilson's disease and pseudosclerosis.

(3) Focal lesions in the cerebral cortex, characterized by a prolific vascular new formation, are described.

(4) A selective necrobiosis of the large motor cells of the putamina and caudate nuclei was found histologically.

(5) It appears probable that:—

- (*a*) An early stage in the destruction of nervous tissue in these diseases is the development of a specific type of vascular new formation.
- (*b*) The changes described in the lenticular nuclei in the case reported represent a late stage in their degeneration.

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RHYTHMICAL CONVERGENCE SPASM OF THE EYES IN A CASE OF TUMOUR OF THE PINEAL GLAND.

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THE study of the symptomatology of tumours of the pineal gland has brought to light a great many facts, but there is still much to be learned. It is, therefore, necessary that all cases that may contribute to a fuller knowledge of this subject be described, and for this reason I record here a case with remarkable clinical symptoms:—

H. K., aged 14, came of a neuropathic family. A sister of the father's was epileptic; the paternal grandfather indulged in alcohol to excess, and the mother and maternal grandmother were abnormal. A brother of the father suffered from tuberculosis. The parents are healthy and have had two children only; there were no miscarriages. The patient's brother is healthy. The patient's birth was attended with difficulty, instruments being used, but, as far as can be ascertained, no permanent bad consequences ensued. The child's development was normal; he learned to walk and speak at the normal time, and he was clean in his habits at an early age. He did not suffer from nocturnal enuresis. He has had no serious illness and was not subject to fits. He was a gentle, somewhat nervous boy, who did not get on very well at school, partly because he was playful and inattentive.

In December, 1919, he began to look ill, became thin, and complained of a singing noise in his left ear, headaches and dizziness; he often stayed in bed for the day. In January, 1920, there came a sudden change for the worse; his temperature rose to 40° C. and he had violent headaches and loud singing in his ears. The fever gradually diminished, but he remained ill and began to squint. He exhibited a pronounced tendency to undue sleepiness; sometimes he slept all through the day. Gradually the illness took the form it presented in September, 1920, when he came under observation.

He was a rather broad-shouldered but short boy, the shortest but two in his class at school, though he was one of the oldest. He had a flabby appearance with deposition of fat chiefly round the breasts and the abdomen; this was the more striking as he was much thinner than he had been formerly. Since March his weight had increased by 7·5 kilog. There was no swelling of the glands, the pulse-rate was 80 and always regular, respiration was quiet but his temperature now and then rose a little above the normal. Smell was not affected. Vision was ¾ in both eyes, which were emmetropic. The visual fields were concentrically limited in a small degree and in both eyes there was a papillitis, with a swelling of 3½ D. in the right eye and 4 D. in the left. The pupils were equal, of medium size and regular in outline; there was no hippus. The reaction to light was exceedingly slight in the right eye, totally absent in the left; on the other hand the reactions on convergence and to pain could be easily elicited. There was convergent strabismus, which increased and decreased suddenly at intervals, so that a rhythmical spasm of convergence ensued. The converging phase of this movement was rapid, the diverging phase slower. The right eye moved fully into the outer canthus, the left eye not quite so much, but the difference was small. There was almost complete conjugate paralysis of upward and downward movements. Adduction and rotation were undisturbed. He did not complain spontaneously of seeing double, but with the red-green spectacles diplopia appeared to exist, the images being homonymous and their mutual position changing little with change in the direction of gaze. Now one image, now the other was slightly oblique. The double images separated further when the object that was to be focused was moved to a greater distance for him. Sensibility in the area of the trigeminal nerve was undisturbed, and the corneal reflexes were present on both sides. The right masseter and temporal muscles contracted less vigorously than those on the left side. The jaw reflex was diminished, and the floor of the mouth was possibly somewhat softer on the left than on the right side. The left side of the face seemed slightly paretic but the facial muscles reacted normally to electric stimulation. There was some diminution of hearing on the left side with shortened bone conduction, while Weber's test showed some lateralization towards the right; this may have been due to slight sclerosis of right tympanum. Rinne's test gave a normal result on both sides. Taste was unaffected. The left side of the pharyngeal arch was somewhat broader than the right, but both moved equally well. Phonation was normal but speech was impeded, slow and scanning. The sternomastoid and the trapezii muscles contracted well. The tongue protruded straight and there was no lingual tremor. There was nothing particular to be observed in the teeth and palate; the pharyngeal reflex was present. The thyroid gland was not enlarged.

It is remarkable that the patient never kept his head still; it was continually in a slight irregular motion. There were no disturbances of sensibility on the neck or chest. No abnormalities in the heart or lungs, or enlargement of the thymus could be detected. The movements at the neck and the spine were free. There was no pronounced dermography or hyperæsthesia. There were incessantly small irregular movements of both arms while they were at rest, and involuntary movements, producing a form of intention tremor or atasia, in movement which gave a certain clumsiness to more delicate actions, as tying knots or writing. Muscular power was poor, slightly less in the left than in the right arm (the boy was right-handed). Muscular tone was normal. There was slight dysdiadochokinesia in the left arm, but no deviation in the pointing tests. The tendon and periosteal reflexes were diminished, and equally so on both sides. The sense of touch, pain, cold, heat, and the sense of position and stereognosis were not impaired. The abdominal organs presented nothing worthy of mention. The right lower abdominal reflex was diminished. Sensation on the skin of the abdomen and loins was not impaired. Both the penis and the testicles were remarkably small, and the growth of pubic hair was scanty. The cremasteric reflex was present. The legs, as the arms, were never still. The strength of both was good, there was no ataxy and the tone of their muscles was normal. The knee-jerks were brisk and equal but there was no clonus. The reflexes of Babinski, Oppenheim and Rossolimo could not be elicited. Sensation was undisturbed in the lower limbs. He could bend the body backwards and raise it again to the sitting position with crossed arms. Romberg's phenomenon was absent. He walked and stood unsteadily.

The urine contained no albumen, and no sugar even after taking 100 gr. of glucose on an empty stomach. The reactions of Wassermann and Sachs-Georgi (Bok's quantitative method) gave repeatedly negative results in the serum and cerebrospinal fluid, as well as in the blood of both parents. Nonne's reaction was sometimes faintly positive ; Pandy's reaction was often so. The cerebrospinal fluid contained 40 cells per c.mm. ; these were lymphocytes and plasma cells. Micro-organisms were never found and guinea-pigs injected with it did not develop tuberculosis. Its pressure was on an average 50 cm. of water. These values were pretty regularly found in the frequent lumbar punctures which were made for therapeutic purposes. Von Pirquet's reaction was weakly positive. The cell count in the blood was about normal. No abnormalities were detected in radiographs of the cranium and the sella turcica was not enlarged. Examination of the labyrinthine reflexes by Bárány's methods elicited strong reactions and the patient soon began to vomit. This, added to the rhythmical convergence spasm of his eyes, rendered examination exceedingly difficult and unreliable.

He exhibited no defects of intellect, though he was emotional in a high degree and cried readily. He did not suffer much from headaches and seldom vomited.

In coming to a clinical diagnosis we were influenced by the following considerations : There must exist a localized process in the skull, the nature of which it was not possible to determine with certainty. Lues could be excluded with probability, but we could not decide between an inflammatory process or a tumour. The neurological symptoms suggested that the disease involved the corpora quadrigemina. The following considerations led to this conclusion : there was a typical conjugated paralysis of upward and downward movement of the eyes ; Argyll-Robertson's symptom which has been found in quadrigeminal tumours (Kinnier Wilson [47], Bruns [10], Rorschach [39] and others) ;

light auditory disturbances; the general motor and static unrest might be regarded as a mild form of the choreic and athetotic movements which occur in quadrigeminal affections. The disturbances of equilibrium in standing and walking, and the affection of co-ordination of the more delicate movements, reminded us of the combination of intention tremor, ataxy and athetosis described by v. Oordt [36]. The somnolence, which had been present in the beginning of the illness, and the disturbances of speech also pointed in the same direction. There were, however, indications that the disease had already extended caudalwards and ventralwards; the slight paresis of the face and the involvement of the root of the trigeminal nerve might be attributed to this. After the operative decompression which was performed later, the paresis of the jaw disappeared, hence I assumed that the lesion of the trigeminal nerve was due to increased cerebral pressure and compression of the ganglion Gasseri and the third branch of the nerve against the petrous bone, as in the case described by C. F. van Valkenburg [45]. In addition to these neurological signs there was a tendency to adiposity and an exceedingly small development of the penis and the testicles, that is a type of a dystrophia adiposo-genitalis which was regarded as secondary to distention of the third ventricle. Jelliffe and White [28] described the occurrence of dystrophia adiposo-genitalis in cases of hydrocephalus internus with closure of the aquæductus Sylvii. Consequently the clinical diagnosis was a morbid process which destroyed the corpora quadrigemina.

It was possible to confirm the diagnosis after death, though the brain was removed under very difficult circumstances. An account of the autopsy follows.

After the dura mater and the falx had been removed from between the hemispheres a tumour of the size of an almond was found at the place where the falx and the two halves of the tentorium cerebelli join. This tumour had a short stem on its anterior side which was torn through. No disease could be detected in the soft meninges. The cerebral gyri were broad and flattened, and the sulci were narrow. There was a hydrocephalus internus with pronounced widening of the lateral and the third ventricles. In the situation of the epiphysis and the corpora quadrigemina a tumour mass was found of the size of a nut, which extended dorsally and bent round the splenium of the corpus callosum, presenting there a severed stem, which evidently was connected with the stem of the tumour removed with the dura. The upper pole of the cerebellum was flattened by the tumour, and the thalami had been pressed aside. The tumour in the hard meninges was fairly firm, sharply separated from its surroundings and of a regular form; that in the position of the epiphysis on the other hand was loose, soft, friable and irregular in shape. It was connected with the tela choroidea. Though the two tumours did not resemble each other macroscopically, and if they had not been clearly connected by a stem one would have been inclined to assume two mutually independent growths, yet under the microscope all parts of the growth appeared to belong to the type of epiphysis tissue which is found in young individuals. In the first place it contained cellular tissue septa, which in the main mass were loose-meshed, and in the dural growth were thin and compact. Between the septa lay irregular groups of polygonal large cells with large pale nuclei, and between them groups of small cells, poor in protoplasm and possessing dark round nuclei. These latter cells resembled lymphocytes. The microscopical picture agreed entirely with that of the outer layer of the teratoma of the epiphysis described by Hymans van den Berg and van Hasselt [27], preparations of which I have been able personally to examine through Dr. van Hasselt's kindness. The rest of the tumour corresponded with the description and illustration which Löwenthal [30] gives of an epiphysis tumour examined by him. Löwenthal regarded his tumour as an " adenoma

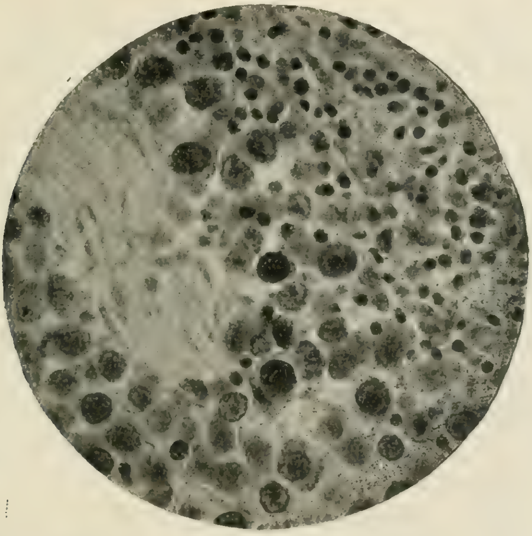

FIG. 1.—Photomicrograph of the tumour.

maligna." Though macroscopically the resemblance to Löwenthal's specimen was very great, the connecting stem with the falx cerebri was absent in his case. I have succeeded in finding this in one case only in the literature, i.e., in v. Frankl Hochwart's remarkable teratoma [18]. The place of attachment was there the same as in our case, viz., the point where tentorium cerebelli and falx cerebri meet. In v. Frankl Hochwart's case there was, however, no tumour tissue between the layers of the dura mater.

In consequence of the difficult circumstances attending the autopsy a complete examination could, unfortunately, not be performed, and the other organs of internal secretion could not be investigated. The hypophysis was not examined.

This case of epiphysis tumour presented many points of interest; it may be compared with other cases recorded in literature.

In the first place the movements of the eyeballs must be discussed at more length. There was a fairly regular rhythmical convergence, consisting in a rapid phase of convergence and a slow phase of divergence. Professor Dr. W. P. C. Zeeman, who examined the patient, was so kind as to allow me to see his notes. He described the phenomenon as "continual abrupt converging of the eyes." The deviations resembled those of a nystagmus of medium degree. The frequency of the oscillations was smaller than those of the nystagmus, about one or two occurring every second. They were not regular in rate, and were best observed when the patient looked straight in front of him without accurate fixation; on intentional focusing the movements continued but were less easy to see.

How should these phenomena, which, as far as I know, have never yet been described, be interpreted? They were undoubtedly related to the existing convergent strabismus which presented some peculiar characteristics, for the double images hardly changed their relative positions when the patient looked to the right or the left, but they moved farther apart when the object to be focused was moved farther away.

Hence there was here either spasm of convergence or paresis of divergence. It is the more difficult to decide which of the two was present, as ophthalmologists are not agreed on the existence of the latter. Straub [43] states that a paresis of divergence may occur; Bielchowski [8], on the other hand, is of opinion that one is never justified in assuming the existence of divergence paresis. It may, however, be pointed out that the spasm of convergence, if it existed, was not accompanied by disturbances of accommodation or change in the pupils. On the whole little is found in textbooks of neurology on spasm of the ocular muscles. Hysteria is regarded as the most common cause of spasm of convergence, but it occurs also in meningitis. Ophthalmologists devote more attention to it, and others too lay stress on its hysterical ætiology. Straub mentions cerebral tumours and abscesses as causes of paralysis of divergence. Körber's nystagmus retractorius may be mentioned as another form of rhythmical movement of the eyeballs, which cannot be classed with the more generally known forms of nystagmus, and which possibly presents some relationship to the movements in my case. This phenomenon consists in the eyeballs being rhythmically drawn backwards. Bárány [4] describes the phenomenon as present in one eye in a case of a tumour of the corpora quadrigemina. The retraction was synchronous with the nystagmus of the other eye. Elschnig [14] found nystagmus retractorius twice with affections of the aqueduct of Sylvius; in these cases the convergence increased somewhat with the rhythmical retraction of the eyeballs.

Another peculiarity in the eyes was the existence of Argyll-Robertson's sign. Dejerine [13] states in his well known textbook that the Argyll-Robertson phenomenon combined with lymphocytosis of the cerebrospinal fluid is pathognomonic of syphilis. This rule appears, however, not to hold good in this case, and accordingly not to be of universal validity.

Another point of interest is the nature of the trophic disturbances. These were certainly not typical of an epiphyseal tumour; the genitals were small rather than large, the growth of genital hair was not excessive, nor was the amount of hair on the body exceptional. He was also rather small for his years, and there was no extraordinary precocity in his mental development. Why did the syndrome of macrogenitosomia præcox, so typical of epiphyseal tumours, not exist in our case? As early as in 1909 Marburg [32] surmised that the pineal gland has an internal secretory function, which normally inhibits the development of the genital organs. This standpoint has been made more plausible by subsequent clinical observations, and the animal experiments by Foa [19] point in the same direction. He found after the removal of the epiphysis in cocks a hypertrophy of the secondary sexual characters. Similar experiments were performed in mammals by Sarteschi [40] with the same result. Other investigators, however, as Dandy [12] and Exner and Boese [15], could not confirm Sarteschi's results.

Askanasy's theory [1] is opposed to the hypothesis that a disturbance of internal secretion is the cause of the trophic disturbances. He takes the view that the trophic disturbances are dependent on the tumour itself. He is of opinion that all epiphyseal tumours accompanied by hypergenitalism which have been examined, consisted of embryonic tissue; the cases of Ostreich-Slawyk [37], Holzhäuer [25], Goldzieher [23] and Ogle [35], were not sarcomata as the authors erroneously assumed, but teratomata or allied chorioepitheliomata. It is only for Raymond and Claude's case of glioma [38] that Askanazy cannot account. He rests his theory on the fact that teratomata in other parts of the body have occasionally caused hypergenitalism. He considers the existence of a teratoma as a kind of "gestation," which may give rise to a peculiar development in a boy. All things considered Askanasy's view does not seem very plausible, and the fact that there was no teratoma or epithelioma present in our case does not explain why the syndrome of macrogenitosmia præcox was not present. I would rather attribute the cause to our patient's age, for though it is certainly not true that trophic disturbances do not appear after the seventh year as Marburg assumed, there is an age limit which seems to lie about the twelfth year; only Goldzieher's case [23] is an exception.

The following table records the ages of the cases of epiphyseal tumour with macrogenitosomia præcox, which were anatomically confirmed.

Goldzieher [23]	16 years,	angioblast sarcoma
Bailey and Jelliffe [3]	12 ,,	teratoma
Raymond et Claude [38]	10 ,,	glioma
Takeya [44]	10 ,,	teratoma
Odermatt [34]	10 ,,	teratoma
Boehm [9]	9 ,,	teratoma
Hymans v. d. Berg en v. Hasselt [27] ..	8 ,,	teratoma
Gutzeit [24]	5 ,,	teratoma
Steiner und Johan [42]	7 ,,	adenoma
Ogle [35]	6 ,,	alveolar sarcoma
v. Fränkl-Hochwart [18]	5 ,,	teratoma
Holzhäuer [25]	4 ,,	sarcoma
Ostreich-Slawyk [37]	4 ,,	psammo-sarcoma

When we contrast with these cases those of teratoma in which macrogenitosomia did not occur, we see that the age was then always 12 years or more.

Gauderer [21]	12 years
Coats [11]	13 ,,
Weigert [46]	14 ,,
Falkson [16]	16 ,,
Hueter [26]	19 ,,
Fukuo [20]	19 ,,
Schmincke [41]	22 ,,
Neumann [33]	27 ,,

It follows from these facts that macrogenitosomia cannot be expected to develop in a boy of 13 years. Nevertheless all symptoms of disturbance of internal secretion were not absent, for there were unmistakable indications of dystrophia adiposo-genitalis. This syndrome occurs sometimes with epiphyseal tumours (Jelliffe and White) [28]. But the question has not been satisfactorily decided yet in how far the disturbance of the epiphyseal function can cause adiposity. It is certainly not constantly associated with typical macrogenitosomia præcox. Falta [17], Cushing and others, consider adiposity to be a hypophyseal phenomenon which has nothing to do with an internal secretion of the epiphysis. In our case, where a complete hypophyseal picture existed, this view seems very probable, since the hypophysis would be hampered in its function by the dilatation of the third ventricle which compressed the infundibular region. This interpretation seems the more plausible, since Frölich's syndrome is also found in cases of tuberculosis of the floor of the third ventricle, and in a case of injured infundibulum with intact hypophysis Lereboullet, Mouzon and Cathala [29] found the condition of dystrophia adiposo-genitalis. It is still, however, remarkable that as a rule no adiposity co-exists with ordinary hydrocephalus, though cases are known in which it did occur (Goldstein [22]). It may be that the pressure relations due to a tumour of the mesencephalon producing closure of the aqueduct of Sylvius and pressure on the blood-vessels of the choroid plexus, is different from those of an ordinary hydrocephalus. These views are in conflict with Marburg's hypothesis, which attributes the adiposity to hyperpinealism. Marburg's theory, however, does not seem probable since it is hardly possible to assign a specific hyperfunction to the glioma that existed in Raymond and Claude's case.

Summarizing the special features which this adenoma of the epiphysis presented, we see :—

(1) There was rhythmical spasm of convergence.

(2) There was Argyll-Robertson's sign with lymphocytosis of the cerebrospinal fluid, not due to cerebrospinal syphilis.

(3) The disturbances of internal secretion were the same as those found with dystrophia adiposo-genitalis.

(4) The tumour consisted of two parts connected by means of connective tissue, one part lying in the situation of the epiphysis, the other part between the folds of the dura mater where the falx cerebri and the tentorium cerebelli meet.

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THE INFLUENCE OF THE CEREBRUM AND CEREBELLUM ON EXTENSOR RIGIDITY.

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INTRODUCTION.

THE condition of decerebrate rigidity which manifests itself as a prolonged and enduring contraction of the extensor muscles, especially those which oppose the action of gravity when the animal is standing, was shown by Sherrington [7] to result from decerebration at the level of the mid-brain. It is readily produced experimentally in the higher mammals, cat, monkey, &c., by the ablation of the cerebral hemispheres. Sherrington found that if he removed only one hemisphere the rigidity appeared to be rather inconstant in its production and non-persistent, but was perhaps more marked on the ipsilateral side. He further showed [8] that decerebrate rigidity is abolished when the continuity of the proprioceptive reflex arcs is interrupted. The afferent path of these reflex impulses ascend to the brain by way of Gowers', or the ventral spino-cerebellar tract, and not by the dorsal columns, since the rigidity is unaffected by cutting the latter. The efferent impulses do not pass by way of the pyramidal tracts, but appear to descend in the cord by some tract originating in the region of the red nucleus. Sherrington [10] considered that the cerebellum was not an essential link in the production of decerebrate rigidity, since this condition often remained after the removal of the cerebellum.

Thiele [11] attempted a further analysis with the idea of discovering the tracts, centres and place of origin in the brain of the impulses leading to decerebrate rigidity. He came to the conclusion that this condition is not due to the removal of the cortical influence, but of a thalamic one; and furthermore, that this thalamic influence is transmitted along a tract which decussates high up in the mesencephalon. The result of cutting this tract far forwards, therefore, is rigidity on the opposite side of the body, while a section posterior to the anterior corpora quadrigemina gives ipsilateral rigidity accompanied by slight contralateral rigidity. Thiele found that the cerebellum exerted an influence on decerebrate rigidity, since extensor rigidity appeared after each of the following operations: removal of the tentorium, division of the vermis, unilateral ablation of the cerebellar cortex. Rigidity could be abolished by destroying the dentate nucleus or by cutting the trapezal fibres in the pons. The results of his experiments led him to express the view that there are two antagonistic forces acting on the ventral horn cells of the cord; one from the thalamus exercising an inhibitory influence upon the contralateral side, the other from Deiters' nucleus exercising an augmenting influence; an indirect control may be maintained by the cerebellar cortex, since it exerts an inhibitory influence on Deiters' nucleus.

Weed [12] concluded from his experiments that the main centre and the source of decerebrate rigidity lay in the red nucleus in the mid-brain. The work of Magnus [3] and Bazett and Penfield [1], however, has proved that the red nucleus is not the centre for decerebrate rigidity, since rigidity persists after transection of the brain-stem posterior to this nucleus. Bazett and Penfield locate the centre for decerebrate rigidity at the level of Deiters' nucleus.

According to Weed there are two inhibitory influences acting on the dentate nucleus, one from the cerebellar cortex, as Thiele, and more recently Miller and Banting [5], have shown, the other from the cerebrum. The course of this latter tract was shown definitely to lie in the mesial anterior fraction of the internal capsule above the thalamus, and in the mesial fraction of the crura cerebri. Thus the inhibitory pathway cannot originate in the thalamus as Thiele had supposed, but it apparently arises from the cerebral cortex. Weed demonstrated that it runs caudad in the mesial part of the internal capsule, and inferred that its fibres ended in the pontile nuclei. The tract passes eventually to the cortex of the cerebellum by way of the contralateral middle cerebellar peduncle. Sherrington [9] had suggested such a tract earlier.

The apparently contradictory results—namely, that in one case ipsilateral and in the other contralateral rigidity was produced by unilateral cerebral ablation—Thiele explained by the difference in level of the section, ipsilateral rigidity resulting if it were at a high level and contralateral rigidity if at a low level. Weed, on the contrary, found that ipsilateral rigidity resulted no matter at what level the section was made.

Our object in this investigation was the discovery, if possible, of the exact location of the inhibitory pathway, and the effects produced by its destruction at various levels.

EXPERIMENTAL RESULTS.

(1) *Technique.*—All our experiments were performed on cats, and no experiments reported here were survival experiments, i.e., the results were obtained within twenty-four hours after the first operation.

The animals were deeply anæsthetized and a tracheal cannula inserted, after which anæsthesia could be continued, or artificial respiration given. In the first few experiments the carotid arteries were tied previous to any operation on the skull. This practice was soon discontinued because it was found that in certain animals the mere interference in this manner with the blood supply to the brain produced a marked degree of extensor spasm.

In disclosing the brain an ordinary trephine, $\frac{3}{4}$ in. in diameter, was used. Hæmorrhage was controlled by the application of wax to the cut edges of the bone, and of hot saline packs over the whole area of operation. No serious hæmorrhage was encountered in a series of forty animals, so that any lack of extensor rigidity was never caused by an enfeebled condition consequent upon the loss of blood. The brain could be kept in an excitable condition only by the continued application of warm saline sponges. This procedure was found to be most important, for unless the circulation in the choroid plexus remained good, the cerebral cortex quickly became inexcitable (cf. Miller and Banting).

There are several other factors besides the tying of the carotids which have an effect on extensor muscle tone. Chief among these is the position in which the animal is lying, especially the relation of the head and neck to the rest of the body (Magnus and Kleijn [4], also Bazett and Penfield, p. 197). If the animal is lying on its side with its head raised, the limbs on the side of the body in contact with the table normally exhibit a greater degree of rigidity than those on the other side. This effect can be readily demonstrated by testing the rigidity of the front or hind limbs of a decerebrate cat lying on its left side. The left fore and hind limbs will exhibit greater extensor rigidity than the right ones. But upon turning the animal over on its right side the right limbs become at once the more rigid. Therefore when a test of the degree of rigidity was being made in an experiment the animal was suspended on its abdomen in a trough and the position of the limbs noted as they hung freely in the air, or still better a comparison was made of the force necessary to bend the right and left legs at the knee or elbow when the animal was suspended in the trough or lying flat on its back. In the latter case a spring balance was sometimes used to register the number of pounds of pressure necessary to cause bending of the limb. This varied from a few ounces to $3\frac{1}{4}$ lb., depending on the state of extensor tone. Ether anæsthesia also profoundly affects muscle tone. If the animal is lightly etherized it shows marked extensor rigidity very similar to, if not identical with, decerebrate rigidity. Ether rigidity, however, is always bilateral and is fairly transient, probably due to inability to maintain a constant degree of anæsthesia; also it is often interrupted by clonic movements. Sometimes ether rigidity was purposely induced for experimental reasons, but when such a condition might obscure rigidities of other origin, the animal was allowed to come completely out of anæsthesia before the rigidity was tested, or the anæsthesia was deepened until the ether effect had disappeared, but rigidity due to nervous lesions persisted.

In cutting parts of the cerebrum, the cerebellum, or their peduncles, a very sharp scalpel was used, but if the incision had to go far into the cranium and there was danger of injury to the venous sinuses, a blunt instrument was employed.

For cortical or nerve tract stimulation a unipolar stigmatic electrode was used. A large zinc plate applied to the back of the animal and covered with gauze moistened with saline served as the other pole. The source of stimulation was an interrupted current from an inductorium. The strength of the current was not measured, but it was just strong enough to cause contraction of the scalp or jaw muscles when applied directly to them. When the cortex or cut surface of the brain was dry the effect of the stimulus could be noted almost immediately, but if there was hæmorrhage five to fifteen seconds often elapsed before stimulation became effective. No currents strong enough to spread to the jaw, scalp or neck muscles were used.

(2) *Influence of cerebrum.*—These experiments were undertaken with the object of ascertaining the effect of high and low section of one cerebral hemisphere, and of tracing to the cortex, if possible, the inhibitory tract found by Weed in the mesial part of the internal capsule. The first experiments to be described are those which resulted in the production of extensor rigidity.

In some fifteen cats marked contralateral extensor rigidity of fore and hind legs followed the ablation of the whole of one cerebral cortex anterior to the optic thalamus. (The results obtained are similar to those described in Cat 53.) The rigidity was quite persistent both during anæsthesia and also when the animal was fully out, except during the mimetic walking movements which always occur at frequent intervals after this operation. The thalamus in these cats was still intact, and although mimetic movements may possibly originate from lower segments, they never persist unless the thalamus remains. The ipsilateral side often showed some slight increase in extensor tone, but this was inconstant and not marked. No rigidity of the neck or tail was noted under these conditions.

Further section caudad by successive slices through the thalamus did not increase the rigidity, but in one cat section of one cerebral hemisphere just below the level of the anterior corpora quadrigemina produced ipsilateral rigidity with very slight increase in tone on the contralateral side. The rigidity thus produced was similar in character to that produced by high cerebral ablation, in that it was not as constant or marked as the rigidity produced by removal of both cerebral hemispheres, but differed in that it was chiefly ipsilateral. This bears out Thiele's statement that the question whether ipsi- or contralateral rigidity shall result after removal of one cerebral hemisphere depends upon the level at which the cut is made.

Cat 58.—9.30 a.m. anæsthetized. Trephined over left occipital lobe. Cut down through left cerebral hemisphere just posterior to anterior corpora quadrigemina to base of the skull. Did not remove this part of brain, but left it inside skull. Ether discontinued.

10.15 a.m.: Cat raises head. Rigidity on both sides, but much more marked on left side in both front and hind limbs.

10.20 : Claws with left front leg violently. Left front leg then becomes very rigid. Both front legs now become flaccid.

10.24 : Rigidity returned in all four legs. Left legs more rigid than right. Cat raises itself off the table.

10.40 : Suspended in trough. Left legs more rigid than right, and more difficult to pull out when forced into position of flexion, i.e., some spasticity on left side.

10.45 : Ether given again.

The motor area in the cerebral cortex in several cats was mapped out by unipolar stimulation, and it was found to correspond very exactly with the area described by Campbell [2], i.e., the region surrounding the sulcus cruciatus (fig. 1). Definite flexor and rarely extensor movements of the contralateral limbs could be elicited. Stimulation of the cortex just ventral to the sulcus elicited flexion of the opposite fore leg. Slightly more lateral stimulation elicited flexion of toes of opposite fore leg ; still more lateral elicited flexion of opposite hind leg ; stimulation above the sulcus gave extension of the opposite fore leg. When the motor area was cut away to a depth of 5 mm. below the surface on one side, there was no increase in extensor tone on either side of the body. If, however, the frontal area which lies ventral and slightly medial to the motor area was also removed, definite rigidity developed at once in the contralateral fore and hind legs.

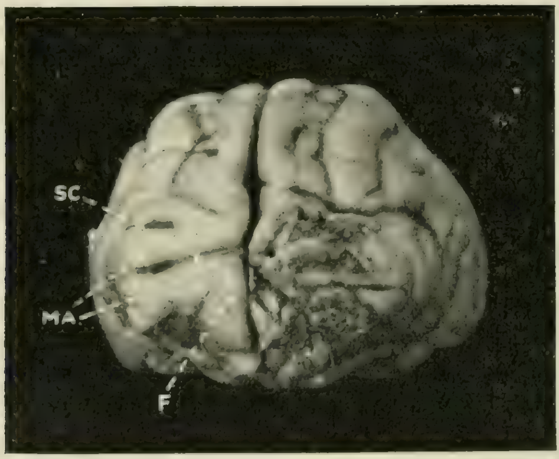

FIG. 1.—Photograph of brain of cat No. 56. S.C., Sulcus cruciatus ; F, Frontal lobe ; M.A., Motor area.

Cat 55.—Anæsthetized. Trephined over left motor area ; tested surface of motor area, and it gave flexion of right leg. Part of left motor area now removed. Cat out of ether and no rigidity in either front or hind legs. Etherized and made a second cut to mid-line on left side, removing all of motor area. Cat out of ether. No rigidity developed. Frontal area found to be still intact. Anæsthetized, and a third deep slice made on left side. Decerebrate rigidity at once on right side. Frontal area found to be removed. Stimulated cut surface of motor area, flexion of right hind leg.

If the frontal area alone was removed, contralateral rigidity resulted, even though the motor area, as shown by stimulation, was still intact. The rigidity resulting from removal of frontal areas may be masked by the voluntary movements which are possible because of the presence of the motor area ; deep anæsthesia does away with these movements and leaves the extensor rigidity evident.

Cat 53.—10.20 : Anæsthetized deeply. Trephined on left side. No rigidity as result of trephining.

10.35: Stimulated cortex near sulcus cruciatus, contralateral fore foot flexed.

10.37: Cut through anterior part of left frontal lobe. Rigidity at once in right fore limb and to a less degree in right hind limb.

10.50: Motor cortex responds to stimulation; also mimetic movements with all four feet occurred, because animal is coming out of ether.

10.51: Both fore legs now rigid, ether rigidity. Stimulated cut surface of left frontal lobe, right fore leg immediately goes limp, not flexed. Left leg unchanged in rigidity, motor cortex still excitable. Nearly a minute necessary to restore rigidity in right leg. Ether discontinued. Cat out of ether. All four legs move actively.

11.9: Etherized until ether rigidity developed again. Stimulated cut surface of left frontal lobe. At once rigidity disappears from right fore leg.

11.10: Motor cortex excitable. Ether discontinued.

11.12: No rigidity when out of ether. All four legs capable of voluntary movement. Observations repeated in the next few minutes.

Extensor rigidity therefore appears after operations on the cerebral cortex only if the frontal area has been injured.

The results of our experiments on modifying the degree of rigidity, once it has been produced, are as follows: If extensor regidity had been produced by removing both cerebral hemispheres just posterior to the anterior corpora quadrigemina, stimulation of the cut brain-stem on the one side produced an immediate cessation of rigidity on the *ipsilateral* side. But if rigidity had been produced by removing both cerebral hemispheres anterior to the anterior corpora quadrigemina, stimulation of one cerebral peduncle was found to give two distinct effects. If the stimulating electrode was placed on the lateral side of the peduncle, movements of the contralateral limbs were produced, i.e., the pyramidal tracts were evidently stimulated. These movements consisted in vigorous flexions, or sometimes rhythmic extension and flexion. If, however, the electrode was placed on the mesial side of the peduncle no movements occurred, but on the *contralateral* side the extensor rigidity immediately disappeared. At first it was thought that this disappearance of extensor rigidity resulted as an act of flexion, but this was not the case, as this limb merely went limp, and all the muscles became flaccid. The limpness remained for 5 to 10 seconds after removal of the stimulus before the muscles regained their former extensor tone.

When one cerebral hemisphere had been cut away above the thalamus and contralateral rigidity was therefore present, stimulation of the outer part of the internal capsule elicited movements of flexion and extension in both fore and hind limbs on the contralateral side. If, however, the mesial part of the anterior limb of the internal capsule was stimulated, the *contralateral* fore and hind limbs became limp, returning to their former state of rigidity shortly after the stimulus was removed. Similarly if the motor and frontal areas of the cerebral cortex on one side were removed, points were found on the more posterior parts of the cut surface which gave contralateral movements, and on the more anterior and mesial parts, a point which invariably gave inhibition of contralateral rigidity. And finally, if the frontal area alone was removed, the motor area being left intact as proven by stimulation, the rigidity on the contralateral side immediately disappeared upon stimulation of the cut surface (see Cat 53). Although the motor and frontal areas are close together there was no spread of current, since the effects of stimulating the two areas were strikingly different, in one case active, forceful flexion or strong rhythmic movements, and in the other passive flaccidity.

The extensor rigidity caused by light ether anæsthesia was used to demonstrate the inhibitory function of the cortex of the frontal lobe. Here also it was found that the rigidity in the contralateral side immediately disappeared upon stimulation of one frontal cortex (see Cat 53).

(3) *The influence of the cerebellum.*—In the course of our experiments we investigated the relation of the frontal inhibitory tract to the cerebellum, and we were able to confirm the following observations made by other investigators. (1) Injury to the cellebellar cortex causes ipsilateral rigidity (Sherrington, &c.); (2) removal of the tentorium on one side produces ipsilateral rigidity (Thiele), probably through injury to the cerebellar cortex; (3) if extensor rigidity is present, removal of one half of the cerebellum, or injury to one dentate nucleus, causes rigidity to disappear from the ipsilateral side (Weed); (4) stimulation of the anterior surface of vermis gives an immediate and general relaxation of rigidity (Sherrington, Miller and Banting, &c.). We also found that if successive sections were made through the mesencephalon in a caudad direction extensor rigidity suddenly disappeared when the region of the posterior corpora quadrigemina was reached. Histological sections taken from the various levels showed that rigidity had disappeared when the cut passed through the pontine nuclei posterior to the red nuclei.

Although the cerebellum does not appear to be absolutely essential for production and maintenance of decerebrate rigidity, since Magnus

[3] and others have confirmed Sherrington's observation that the decerebrate rigidity may appear after total removal of the cerebellum, yet the influence of this organ on decerebrate rigidity is most pronounced, as shown by the results given in the preceding paragraph. It seemed probable, therefore, that the inhibitory path from the frontal lobe might be connected with the cerebellum. The relationship is shown in the following experiments: Rigidity was produced on one side, e.g., the right, by removal of the left cerebral cortex above the thalamus. The cerebellum was exposed without injury to the tentorium and enough of the skull removed to make the right middle cerebellar peduncle accessible. The inhibitory tract was then stimulated and the rigidity in the right fore limb at once disappeared. This was repeated several times, so that there was no doubt that the stimulating electrode was applied to the proper place. The position of the electrode was kept unaltered and the right middle cerebellar peduncle was quickly severed. The inhibitory tract was at once stimulated as before, but there was no effect on the rigidity. This experiment was repeated on another cat with the same result. The inhibitory tract was interrupted by cutting the middle cerebellar peduncle on the side showing decerebrate rigidity. Section of the peduncle on the opposite side did not interfere with the action of the inhibitory tract.

Further proof that the inhibitory tract passes through the middle cerebellar peduncle is shown in the following experiment. The cerebellum was carefully exposed in an etherized cat and the middle cerebellar peduncle alone was cut. The animal at once showed ipsilateral rigidity exactly similar to that produced by unilateral cerebral ablation. Deep anæsthesia was necessary since the cat's voluntary movements when it came out of ether made impossible the detection of increased extensor tone. We did not experiment with the superior and inferior cerebellar peduncles since Weed had already shown that the tracts which run through them do not contain fibres which upon stimulation inhibit decerebrate rigidity.

Summary of Experimental Results.

(1) *Production of decerebrate rigidity.*—Ablation of the motor cortex of the cerebral hemispheres did not result in the condition of extensor rigidity. Rigidity occurred only if the frontal areas were destroyed. If one frontal area was removed, or the cerebral hemisphere cut so that the fibres arising from the frontal lobe and running in the internal capsule were interrupted anywhere in their course down to

about the level of the anterior corpora quadrigemina, contralateral rigidity resulted with slight ipsilateral rigidity. Successive sections through the entire hemisphere did not appear to increase the degree of rigidity resulting after destruction of the frontal area, but the rigidity disappeared when the section passed through the posterior corpora quadrigemina. Hemisection of the brain-stem posterior to the anterior corpora quadrigemina produced mainly ipsilateral rigidity, though contralateral rigidity was also present, but to a less degree.

(2) *Inhibition of extensor tone.*—Extensor rigidity could be inhibited by stimulating at the following points: (1) the cut surface of the frontal lobe; (2) the mesial side of the anterior limb of the internal capsule; (3) the mesial side of the cerebral peduncle; (4) the brain-stem just posterior to the anterior corpora quadrigemina. In the first three cases inhibition of rigidity appeared on the contralateral side, in the fourth case on the ipsilateral side. If extensor rigidity was present, cutting the middle cerebellar peduncle abolished the possibility of inhibiting the rigidity by stimulating at points (1) and (2) on the opposite side to that on which the peduncle was cut.

Ether rigidity could be inhibited by stimulating the intact frontal area on the mesial side of the anterior limb of the internal capsule. The effect was contralateral.

The experimental evidence, therefore, shows that there are tracts in the brain of the cat carrying impulses which tend to inhibit tonic extensor activity, and that decerebrate rigidity results when the influence of the tracts is cut off. The tracts have their origin in the frontal lobes of the cerebral hemispheres. It is to be noted that the tract on one side of the brain does not govern one side of the body exclusively, since there is an increase in tone on both sides of the body after removal of one frontal area, but the effect is predominant on the contralateral musculature. From the frontal lobe the tract passes through the mesial part of the internal capsule and extends caudad past the level of the anterior corpora quadrigemina. It then, in the greater part at least, crosses to the other side of the brain-stem to enter the cerebellum by way of the middle cerebellar peduncle. The tract thus marked out experimentally agrees in general with the so-called "cortico-ponto-cerebellar" path (Ranson, [6], p. 325).

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THE SENSORY ACTIVITIES OF THE SKIN FOR TOUCH AND TEMPERATURE.

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It is a well-known physiological observation, that if the end of a slender metal rod, cooled or warmed to a suitable temperature, be applied lightly to the surface of the skin, a sensation of cold or of warmth is not produced at all points of the surface, but only when the point comes into contact with isolated areas, usually of small size. From the surface between these points a punctate cold or warm stimulus produces no sensation of temperature, and touch alone is felt. The responsive areas or points are known as cold and as hot spots respectively.

Similarly, if the surface of the skin be carefully examined with a fine bristle, pressed lightly to elicit the sensation of touch, or with a firmer bristle, pressed more firmly so as to produce pain, the sensation of pain and of touch are not felt equally everywhere but are especially elicited at small spots termed touch and pain spots.

Based upon such observations, the current view of cutaneous sensation regards the surface of the skin as "a mosaic of tiny sensorial areas each sensitive to a specific stimulus, and the range of ascertained sensitiveness includes the sensation of touch, pain, cold and warmth" (Sherrington [7]).

The discovery by Blix [1], corroborated independently by Goldscheider [3], of this punctate distribution of thermal sensibility was by these writers regarded as an illustration of Johannes Müller's law of the specific energy of nerve fibres applied to cutaneous sensation, and led to the belief in the existence in the skin and subcutaneous tissues of specific structural mechanisms, each subserving one or other form of sensibility, whether of touch, in the form of Paccinian and Meissner's corpuscles, or of cold or warmth, for which other forms of end-organs have been stated to act as receptors.

The theory of special end-organs implied also the existence of special nerve fibres connected with them, and the present view of cutaneous sensation postulates the existence of pain fibres, of touch fibres, and of warm and cold fibres, passing from the special end-organs to the central nervous system.

Sections have been made and examined microscopically of such spots, or fragments of skin which were known to be sensitive to special stimuli, but such search has hitherto failed to demonstrate the presence at such spots of specific end-organs.

The cases of the loss of one or other of these forms of sensibility occasionally found in various regions of the body in syringomyelia and some other spinal conditions, such as a loss of temperature sensation, the loss of touch, or of pain, afforded apparent corroboration of the existence of these separate systems.

Head and Rivers' [4] observations upon the loss of sensation following division of a cutaneous nerve and during its restoration, showed that after such an injury all forms of sensation are not equally lost and are not uniformly restored. Their observations led Head and Rivers to put forward their theory of a dual mechanism of cutaneous sensation, the epicritic and the protopathic, each subserving certain forms of sensation and with special receptor organs and fibres for different forms of sensation.

They deny, however, the existence of a punctate mechanism for all forms of sensation, for in writing of temperature sensation they state that "in the normal skin the hot and cold spots are nothing more than minute areas peculiarly sensitive to either heat or cold, set in a territory over which temperature stimuli can also be appreciated."

The existence of special receptors and special nerve fibres for each of the classical varieties of cutaneous sensation, touch, pain, heat and cold, cannot be considered to be proved, and indeed there are many features of sensation which throw doubt upon the existence of such a mechanism.

In a prolonged series of observations undertaken at the suggestion of Sir James Mackenzie, we have been able to confirm certain facts already known or suspected, and we have observed some others which throw considerable light upon the problem.

The methods employed have been described in the Reports of the St. Andrews Institute [9].

Touch and its Receptor.

Light touch can be excited from all portions of the surface of the body, as well as from certain mucous membranes, such as the conjunctiva and the buccal mucosa. As is well known, it is best elicited in a pure form by contact with a fine brush or wisp of cotton wool, while on hair-containing parts the movement of a hair sufficient to cause motion of the portion embedded in the hair follicle gives the characteristic touch sensation.

Deformation of the surface is believed to be the stimulus effective for the production of the sensation. Examination by the binocular microscope of a portion of skin while it is being stimulated by a fine bristle, so as to produce the touch sensation, shows that the deformity necessary is of the very slightest character, and almost imperceptible. By such examination the surface of the epithelium is seen to have a somewhat unexpected character ; it might be supposed that the surface would show a certain rigidity, but in response to a light touch it is seen to be very mobile—e.g., over the tips of the fingers—and its surface behaves like an extremely thin membrane floating upon a fluid.

Differences of opinion exist as to the mechanism of touch receptors, but it is usually stated to be a function of specific "tactile corpuscles" and their nerves, while the inter-epithelial nerve fibres are stated to convey impulses which give pain sensation.

The terminal branches of superficial nerves end, some in certain specific end-organs, while others pass to the epithelium and terminate among or even in the cells of the deeper layers.

It seems advisable to describe shortly the position of some of the common "end-organs." There are, in man, probably no "end-organs" in the epithelium of the skin, the only form of end-organs which have been described as occurring in epithelium being the Merkel's "touch cells" in the snout of the pig.

These touch cells are large vesicular cells, probably epithelial in origin, lying in groups in the deeper layers of the epithelium, and with a network of neuro-fibrils in close relation to them.

Apart from these, the epithelium is richly provided with nerve fibres, which ramify and form a plexus in its deeper layers.

Nerve impulses are not readily produced by direct mechanical stimulation of nerve fibres; under ordinary conditions they are produced by the activity of receptor organs, and the arrangement in the skin suggests with the greatest probability that touch is not excited by direct mechanical stimulation of these fibrils by deformation of the surface, but that the epithelial cells are receptor organs, which are excited by contact and transmit to the nerve fibrils a stimulus which originates a nerve impulse in them.

The "touch corpuscles" of various types lie for the greater part in the subcutaneous tissues (Paccinian bodies), &c., or in the true skin—and of the latter group, Meissner's corpuscles lie most closely to the surface, occurring as they do in certain of the papillæ of the skin, while other papillæ contain capillary loops.

The distribution of such bodies shows conclusively that they cannot be the sole agents to act as receptors for touch.

Meissner's corpuscles are far too widely scattered in many regions to afford the necessary mechanism—for example, on the volar surface of the forearm one such body was found by Meissner present in 35 square millimetres.

The Paccinian bodies are still less fitted to perform such a function, and their distribution suggests an entirely different use. They are found sparsely scattered in some superficial regions, and exist in considerable numbers in such tissues as periosteum, in the mesentery of the cat, &c., regions from which tactile sensation is entirely absent.

We examined the sensory activity of the exposed surface after removing different thicknesses of skin by blister. The pellicle of a blister is composed of a variable thickness of epithelium, including the stratum lucidum and more or less of the underlying layers. After a short application of a fly blister and in "occupational" blisters the pellicle may contain only the more superficial layers, but after prolonged application the greater part and even the whole of the epithelium may be removed.

When a distinct film of epithelium is left, the exposed surface is dry, and touch can be felt from it, but when more of the epithelium has been removed and the surface is raw and moist, no tactile sensation can be elicited, and pain only is excited by the stimulus.

The inference from the structural and from experimental evidence is that the epithelium of the skin is the receptor organ for the sensation of touch, performing the function of transmitting the stimulus excited by touch to the nerve terminals which are found among the cells of the deeper layers.

Temperature Sensation.

The activity of the cold and warm spots presents peculiar features, some of which have been from time to time recognized by various observers. The first peculiarity to present itself is the extreme difficulty found in enumerating the number of responsive spots present in a given area.

Goldscheider [3], who has been probably the most extensive writer on this subject, has pointed out that at a single sitting a true picture of the temperature spots is not obtained, but that the examination must be carried out for several days if all the spots are to be discovered.

Boring [2] states that it is one thing to map an area in a single investigation for cold or warm spots—it is quite another thing to find these spots a second time and not to find new ones.

The same difficulty was encountered by Trotter and Davies [8] in their observations upon cutaneous sensation in connection with the division of nerves, and Head and Rivers [4] have drawn attention to the varying number of such responsive spots at different observations. Closely connected with this is the variability of situation of the spots, and their ready exhaustion by stimulation.

Our observations established the following facts:—

(1) In different persons there is a very wide difference in the number of cold and warm spots which can be detected at any one observation. In an area of the same size (5 cm. by 2·5 cm.) it was found, for example, in one person that the number of cold spots which could be made out at a single examination varied from eight to eighteen, while in another the number was as great as sixty or seventy.

This difference in number was constant among the individuals, that is, in persons of one group the number was always small, in the other large, but could not be associated with any other condition. The relative numbers of the warm spots followed the same ratio.

(2) Repeated observations corroborate very completely the statement that one or two observations do not disclose the full number of spots within the area from which sensations of cold and of warmth can be elicited, and the sum total of the spots elicited by a number of investigations is vastly in excess of that found at any one time. In other words, under ordinary conditions, of the spots which are capable of giving the thermal sensation, only a fraction are active at one time.

(3) The spots are readily exhausted by a repetition of the stimulus. This is an important phenomenon, but of greater importance is the observation we have made, that dulling of one spot is accompanied by the awakening to thermal sensibility of an adjacent spot. If the point of a fine metal probe cooled to the requisite degree is brought into contact with a cold spot, and the touch repeated again and again at intervals of about a second, at first the contact produces a clear and distinct sensation of cold. After a few contacts, however, the sensation of cold is no longer excited by the stimulus, but that of touch only. The cold sensation may disappear after two or three contacts, or only

after some eleven or twelve, and it may disappear and then reappear once or twice and finally disappear.

If now the stimulus point be moved slightly to one or other side, the sensation of cold is at once set up from a spot from which before no such sensation was elicited.

THE PUNCTATE DISTRIBUTION AND "FLUCTUATION."

The explanation of this varying activity of the spots constituted a puzzling difficulty until we came to realize that we were dealing with a general character of the physiological activity of organs, namely, that under ordinary conditions the whole of an organ is not in a state of activity, but a small part of it only; that there is a coming and going of activity among the different parts—change from activity to quiescence. This feature we have termed "fluctuation," and recognition of its occurrence affords an explanation of many otherwise extremely puzzling phenomena. Some examples may be given.

(1) Fluctuation is very notable at the margins of areas of anæsthesia due to nerve and to spinal injury. In testing the extent of such an area it is a common experience to find that the margin of the area is not the same on two successive occasions—the margin is not fixed, but there is a zone of varying width at one time sensitive, it may be to all forms of stimulation, while at the next examination it may be insensitive. Perhaps more commonly the reverse is found, and the marginal area, formerly anæsthetic, is on a second examination sensitive.

(2) Such fluctuation is also found very notably at the margins of areas of hyperalgesia, whether cutaneous or deeper, and it is almost the rule to find the margin varying at different examinations. Recognition of such fluctuation in these areas was made by Sir James Mackenzie in 1883 [6], and the first record of it is as follows:—

"Towards the end of January, 1881, the patient became worse. He then exhibited the phenomena of hyperæsthetic bands encircling the abdomen, the hyperæsthetic portion on the left side being broader and a little wider than that of the right. The bands could not be distinctly mapped out owing to the variability of the impressions produced. Thus having enclosed, in ink, spaces where the patient declares he feels the pricking of a pin much less than natural, I proceed to other places. On returning to the first spaces I find from his starting and exclamation of pain that they have become hyperæsthetic. The dulled impressions are all either in the upper part of the hyperæsthetic area or slightly above, where they occasionally intermit with the natural about the level of the ninth rib on the left side and the tenth on the right.

"I have been unable to map out the areas on account of the extreme variability of the impressions."

(3) Sensory change and capillary change. The changes in the sensory activity of the "spots" suggested to us that there might be an associated variation in the capillary field. Evidence of the occurrence of such variation is easily obtainable in the condition, common among young adults, in which the fingers and hand are of a purple colour, made up of areas of a deep purple, and of smaller areas of a bright pink colour. If the skin in this condition is carefully watched, it will be found that the margins of the areas are constantly changing, the purple areas encroaching upon the pink ones, while the pink areas die away and new ones appear elsewhere.

Under the binocular microscope the purple areas are seen to owe their colour to a network of small venules filled with blood of purplish colour, and few capillaries can be seen. As the colour alters, small bright red capillary loops come into view in places where none were previously visible.

Examination of an area of normal skin showed that the number and arrangement of the capillaries visible in a given area alter with surprising rapidity.

Capillaries visible at one time disappear from view, and other capillaries make their appearance in the space of a few seconds. The occurrence of such capillary "fluctuation" so similar to the fluctuation in the sensory activity of the normal skin suggests with considerable probability that the two phenomena are causally connected, but of this we have not yet obtained definite proof, as the technical details of the experiments necessary to determine it are extremely complex.

(4) The sensation of itching or tickling shows the same peculiarity. If the surface of the skin on the hairless part, for example, on the front of the wrist, is gently rubbed with a bristle, the sensation of tickling is elicited distinctly from some parts and not from others. If one of these sensitive areas is gently rubbed the tickling sensation gradually disappears, but if the bristle is moved to an adjacent area, usually distal, the tickling sensation is again excited in an accentuated degree.

This gives an explanation of why itching tends to spread by scratching, for the scratching excites the sensitive part and its sensitiveness becomes exhausted, while that of an adjacent area is in turn excited.

(5) Alteration of the vascular condition of the skin produces an extreme modification of its sensitiveness to thermal stimulation. We repeatedly observed the effects produced by applying a mustard leaf so

as to cause an erythema on the sensory capacity of the part, and we found its sensory activity for heat and cold greatly altered. Such a reddened area is not hypersensitive to touch with a neutral body; light touch with the point of a pencil, for example, does not cause pain, but the area is extremely sensitive to warmth. Mild radiant heat, pleasantly warm on unaltered parts of the surface, causes at once a severe pain in the reddened areas.

The first effect of a mild erythema is to alter the sensation resulting from stimulation of the hot spots.

A mildly warm point applied to them gives no sensation of warmth, but, instead, one of sharp pain.

In a more pronounced erythema a further change occurs, and, if such an area is carefully examined for warm spots, a central area is found in which every touch of a warm point produces pain, and around this area is a zone of variable size in which from practically every point of the surface contact with a warm point causes a sensation of warmth. The sensation is not produced only from widely separated points, but from the general surface.

The effect of the erythema is to disturb the "punctate" arrangement of warm spots, and instead of discrete and separated sensitive points, all parts of the surface may become sensitive for warmth.

The principle of "fluctuation" affords an explanation of this phenomenon also. The erythema induced by the mustard leaf has excited to activity all the sensory areas, and all of them respond to the warm stimulus. The effect of the mustard leaf is a "stimulation"—a calling into activity of all parts of the organ stimulated which are capable of activity.

SUMMARY.

The principal results which have been reached include the following:—

(1) There is structural and experimental evidence to show that the epithelium of the skin and of certain mucous membranes is the receptor organ for tactile sensation.

It is not merely a protective covering, but the receptor organ for a special form of sensation, viz., touch.

(2) At single examinations hot and cold spots show a punctate arrangement; the number of such spots in an area of given size however differs widely in different individuals.

(3) On repeated examination of the same area, the number of the hot and cold spots is greatly increased, new spots appearing on successive examinations, while many of those formerly found no longer respond.

These observations harmonize with the results obtained by practically all those who have investigated this subject.

(4) In addition, we find that under certain conditions, such as that of mild erythema, the sensation of heat can be obtained from practically all points of the affected surface at a single examination.

It follows from this that all parts of the surface are potentially sensitive to heat, and that there is no structural punctate arrangement of special receptors and special nerve fibres for thermal sensation.

(5) The punctate distribution of sensitive spots found at a single examination is explained by the view that in the skin there is a constant coming and going of activity of the different parts. Other examples of "fluctuation" are afforded by the skin capillaries in normal and in certain abnormal conditions, and the same principle may form the explanation of the variations found in areas of hyperæsthesia and anæsthesia.

To this coming and going of activity we have applied the term "fluctuation."

(6) The erythema produced by the mustard leaf acts upon the heat-receptive areas in such a way as to abolish temporarily this fluctuation and excites all of them to receptivity.

We do not discuss the bearing of these observations upon Head and Rivers' theory of a dual mechanism of sensation, protopathic and epicritic, each subserving various forms of sensation, but, in our view, the different forms of sensation obtained by these observers indicate differences in the physiological activity of a single mechanism rather than the existence of a dual structural apparatus, each of which is composed of different elements.

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[The fluctuation which is described here in the skin capillaries is amply corroborated by the observations of Krogh [5] which came under my notice after our observations had been made and this paper written.

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THE "LAW OF FLUCTUATION," OR OF ALTERNATING PERIODS OF ACTIVITY AND REST IN LIVING TISSUES.

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In the study of disease which is in progress in the Clinical Institute of St. Andrews we have met with conditions which appear to us to be explainable upon the assumption that the units which make up the structure of the tissues and organs of the body show alternating periods of activity and quiescence. The phenomena are most clearly apparent in the case of the nervous and muscular tissues but are found in others, and appear to be the expression of a property which may be common to living matter generally. This property we term "fluctuation," and by it we mean that the individual units of which the tissues are composed are constantly varying between the two conditions of complete activity and complete rest. Each group of units has its period of activity which is followed by a period of quiescence. The active phase lasts for a while and is succeeded by a period of rest during which other groups are in activity. In this way all parts of the tissue or organ take their share in rotation in the performance of its function, and the activity of the organ as a whole is graded by the number of active units brought into play at any one time. Such an alternation of activity and rest in the units prevents their undue fatigue, is economical in the distribution of work and its resulting wear and tear, and at the same time provides a large reserve of units to meet conditions in which excessive calls are made upon the organ.

The "law of fluctuation," as we are in the habit of terming it, appears to us to be a necessary sequel to the law of "all or nothing," a law which the work of Keith Lucas, Adrian and Forbes has shown to be applicable to muscle and nerve. The phenomena are well known, but the full significance of the law of "all or nothing" in its bearing upon the activity of an organ as a whole has not been sufficiently appreciated. Keith Lucas [9] pointed out that the unit of voluntary muscle, the muscle fibre, when in action always gives a full contraction and shows no gradation, and that the graded activity of the muscle as a whole is effected by the contraction of varying numbers of groups of fibres. Adrian [1] and Forbes [6] have proved that the nerve impulse obeys the same law, the individual nerve impulse showing no sign of gradation. Voluntary muscle is dependent as regards its activity upon nerve impulses which reach it from the central nervous system through its motor nerves. The graded action of voluntary muscle must, therefore, be of nervous origin, and fluctuation of activity and rest in the muscle must be dependent upon a similar fluctuation of activity and rest in the neurones which are concerned in the control of the muscle. The efferent neurones which supply muscle are not automatic, but are actuated, whether voluntarily or reflexly, by nerve impulses reaching them from other neurones. We must, therefore, look to the reflex arc for the explanation of fluctuation in voluntary muscle. The neurones in the reflex arc are conducting elements and are endowed with properties which render it extremely unlikely that they are directly concerned in the production of fluctuation. The receptors which initiate the nerve impulse, the synapses which lie between the neurones in the nervous system and the receptive substance of Langley or the myoneural junction of Elliott, are all parts of the reflex arc which might be subject to influences determining fluctuation. All these structures are specially liable to fatigue and are the parts of the reflex arc which give to the reflex its special characteristics. The increased resistance offered by the receptors to the initiation of nerve impulses, and by the synapses to their passage from one neurone to another, resulting from slight fatigue, may suffice to bring about continual variations in the incidence and outflow of nerve impulses in the central nervous system. Such an explanation of fluctuation seems a natural one, especially when taken into consideration with the important fact that an unfatigable nerve fibre or neurone is served by numerous highly fatigable receptors, synapses and myoneural junctions. The occurrence of fluctuation in the nervous system would seem to be a provision against severe fatigue, and the question at once arises—does a slight degree of fatigue suffice to divert the nerve impulse, or is some other mechanism concerned? Fluctuation is an established fact in many blood-vessels and especially in capillaries. The temporary cessation of capillary blood flow may in some cases be a sufficient explanation of the coming into action and the going out of action of receptors, synapses and myoneural and other junctions. But here again we are faced with the same difficulty as to whether capillary fluctuation is a nervous phenomenon, or an inherent property of the capillary cell. If the latter property be granted to the capillary cell the same property may also be extended to other living structures.

Capillary fluctuation cannot be regarded as an adequate explanation of fluctuation in the receptors of an extravascular tissue such as the epidermis of the skin. Fluctuation in the receptors of the skin can be readily demonstrated, especially in those which are concerned with the reception and translation into nerve impulses of heat and cold, and on general grounds the occurrence of fluctuation would seem to be far from improbable in all receptors which lie in multiples upon branches of any one afferent fibre. It is well known that many afferent nerves branch abundantly near their terminations in the periphery, and that each branch of the axis cylinder has its own receptor or receptors. This is especially well shown in the free nerve endings in epithelia. Even special receptors may lie in multiples upon branches of the same neurone as is illustrated by the Paccinian bodies in the mesentery of the cat, where the branches can be traced to their endings. In accordance with the law of "all or nothing" the nerve impulses initiated by any one receptor are full-sized nerve impulses in the main axis-cylinder. The simultaneous stimulation of any other, or of all the receptors on the same axis-cylinder, will give no greater individual nerve impulse than stimulation of one alone. Indeed, only one receptor can be effective at any one time, for the nerve impulse from it will, by its refractory period, impose a temporary block upon all the other branches. If the branches are not in action the nerve impulse, as in an axon reflex, must descend along them and so increase the block. The difficulty is encountered that we do not know the rate of discharge of nerve impulses by the receptors, and it may be that multiple receptors can furnish a more rapid succession of nerve impulses than can be initiated by one alone. It is possible that the magnitude and even the character of the end-result of stimulation of the receptors depend upon the number of nerve impulses initiated in the neurone in unit time.

We suggest that the multiplication of receptors and branches of the neurone is necessary for the continued action of the nerve fibre, and that they act as relays for the latter. Some such arrangement appears to be requisite to enable an indefatigable nerve fibre to be associated in function with numbers of readily fatigable receptors. Fluctuation of receptors or groups of receptors may be ascribable to fatigue, or to an inherent property of some part of the receptor whereby an alternation between activity and rest is effected.

A similar argument may be applied to the branching of the dendrons of the neurones which lie in the central nervous system. Some nerve cells, e.g. the cells of Purkinje, have an enormous number of dendrites and synapses, and nerve cells in general appear to form many synaptic junctions with other neurones. Many dendrons run for great distances from the cell body, but whether long or short there is no reason to suppose that they do not conform with the laws applicable to the remainder of the neurone. If the law of "all or nothing" is obeyed by the dendrons, one synapse only, and the dendrite or portion of the neurone upon which it lies, should be effective in conducting the nerve impulse at any one time. The synapse may be excitatory or inhibitory in its effect, but, whichever it is, it appears to be effective for the whole neurone. It appears to us that rotation of function or the relay use of the synapses is probable, and indeed may be regarded as necessary for the prevention of fatigue in pathways through the nervous system which are in more or less constant use. Unless some such mechanism be conceived, the non-fatigability of the neurone would be useless, and the strength of the reflex arc would be that of its weakest unit, the synapse.

All neurones show a similar system of branching at their efferent ends. Such branches are of enormous importance because they distribute the nerve impulses and allow of diverse end-results from the same stimulus, as well as varying degrees of gradation in the same end-result. The branches on the efferent side of any neurone must receive all nerve impulses coming to them from the main trunk, and if their endings are equally subject to fatigue one would expect them to be equally affected, so that fatigue is not a likely cause of fluctuation as far as they are concerned. It is conceivable that local conditions, such as capillary fluctuation in muscle, might determine the activity or non-activity of the myoneural junctions.

The assumption of the occurrence of fluctuation in the receptors and synapses of the reflex arc, or of the physiological nerve unit of sensation, provides a simple explanation of many physiological and clinical phenomena. It helps to explain the adaptation which occurs in the various end-organs of sensation, and the persistence of sensation to a continued stimulus.

Varying degrees of excitation and inhibition by excitatory and inhibitory nerves are explainable in the results they produce by variations in the number of groups of units in the organ supplied being brought into activity or thrown out of activity. Drugs and toxins which act upon the nervous system exert their influence upon receptors, synapses or myoneural junctions, increasing or decreasing their sensitiveness and so affecting the passage of nerve impulses through them.

As an illustration of the application of the principle of fluctuation we may take the case of a voluntary muscle, such as the diaphragm, which is in continual action. We have no direct proof that fluctuation exists in the diaphragm and in the nervous respiratory mechanism controlling it, but we are of the opinion that its assumption is a necessity. The diaphragm is capable of great variations in the amount of its contraction, as is shown by the different depths of inspiration which are possible. In ordinary or tidal respiration the contraction is relatively small, but according to the law of "all or nothing" each muscle fibre in it, when contracted, is contracted to its full extent, and gradation of contraction of the diaphragm as a whole must be due to the contraction of varying numbers of groups of its fibres. In a small contraction only a few groups are active, and as more groups come into play the contraction of the muscle as a whole increases. It is unlikely that in the small contraction of tidal respiration, the form of respiration which is of most frequent occurrence, the same groups of muscle fibres are constantly engaged. This would result in a very uneven distribution of the work among the muscle fibres of the diaphragm, and also of the nervous mechanism which controls it. For a maximum effort all parts of the respiratory centre and all the muscle fibres would be brought into action, but the reserve units might be rarely or never used unless there is some system of fluctuation whereby all the units take their share of the ordinary work in rotation.

If there is no such thing as fluctuation in the diaphragm, and in the nervous mechanism controlling respiration, the continual use of the same muscle fibres in tidal respiration must involve the continual passage of nerve impulses through part at least of the same neurones in the respiratory centre, and consequently through the same synapses. Unless these are specially resistent to fatigue we should expect them to show its signs, but we know that no fatigue is manifested in tidal respiration. Haldane [7] has shown that fatigue of the nervous mechanism responsible for the control of respiration can be readily brought about by breathing against a resistance. In breathing against a resistance special effort is necessary, which means that more neurones in the central nervous system and more muscle fibres are brought into action. The fatigue which results manifests itself in rapid shallow breathing which may be very persistent. The condition is seemingly due to fatigue of the synapses upon the nerve pathways in the respiratory centre. The rapid, shallow breathing is explainable on the assumption that the resistance of all the synapses is raised, and afferent nerve impulses in the centre, instead of flowing easily into the efferent inspiratory and expiratory neurones in steady and prolonged alternation, are more rapidly diverted between them.

The occurrence of fatigue from forced respiration, and its persistence when tidal respiration should suffice for the needs of the individual, point to a fatigue of the synapses on the pathways of the nerve impulses concerned in the production of tidal as well as of the deeper forms of breathing. But in tidal respiration the law of "all or nothing" requires the neurones and muscle fibres engaged to have been in full activity, yet no fatigue results. We suggest that in quiet respirations fatigue is avoided in the reflex arc and in the motor nerve endings of the muscle fibres of the diaphragm by the occurrence of fluctuation, there being some mechanism which diverts the nerve impulses controlling respiration to relays of different neurones, and consequently to different groups of muscle fibres. In this way fatigue beyond a certain point necessary to divert the nerve impulses becomes impossible in ordinary quiet respiration. In the respiratory reflex this alternation may be the result of effects upon the receptors, synapses, and possibly the myoneural junctions, in the reflex arcs concerned.

Barbour and Stiles [2] have found evidence that in the sustained reflex contraction of muscle the contraction is maintained by groups of muscle fibres which are continually alternating between activity and rest. Forbes [6] examines this argument in discussing the economy of energy which is a characteristic of muscle tonus, making use of the suggestion that each group of fibres by its activity excites a reflex contraction of other groups in the same muscle, the first group contracted then going out of action because of synaptic fatigue. He states "the fibre groups in this way take up the load in rotation, and, for some reason, by this means attain an economy otherwise impossible." Forbes looks upon this mechanism of rotation as a possible explanation of some of the phenomena of muscle tone, but states that the evidence is insufficient to warrant its acceptance.

It seems to us probable that fluctuation does occur in the maintenance of tone in muscle, and we would ascribe it to alterations in those parts of the reflex arc which are most susceptible to fatigue, namely the receptors and synapses, and possibly the neuromuscular junctions. Fluctuation does not explain the altered metabolism which

Cathcart and Leathes (3) have shown to be a characteristic of tonic as distinguished from the clonic contraction of muscle. The question is not yet settled as to the nature of the muscular contraction in tonus, nor is the exact nature of the nervous mechanism which controls it known.

Fluctuation is very obvious in one form of exaggerated muscle tone which is met with clinically. Irritation of an abdominal viscus brings about a reflex increase of tone in the voluntary muscles of the abdominal wall, which varies from slight resistance of some part of the muscle to the tense contraction of all the muscles of the wall. It is usually, but not always, associated with pain and with hyperæsthesia of the skin or muscle, or both. Fluctuation, as evidenced by a constantly changing area of the hyperæsthesia and of the parts of the muscle contracted, is very common. The phenomena met with are all of the nature of reflex action, and variations in resistance of the receptors to stimulation, and of the synapses on the reflex arc to the passage of the nerve impulse, are regarded by us as the most likely cause of the fluctuation. An increase in the stimulus which excites the condition brings more neurones into action, and possibly increases the frequency of nerve impulses delivered to each neurone by its receptors. The nerve impulses spread in the central nervous system, and may give rise to numerous other reflexes such as vomiting, increased heart rate, alterations in respiration, sweating, pallor, and even shock. The reflexes are usually attended by sensory phenomena of which pain is the most prominent, but depression, nausea, and exhaustion are also common manifestations.

The "all or nothing" law was first established for heart muscle, but it applies to the individual cardiac muscle fibre and not necessarily to the heart as a whole. The heart has a great reserve power of contraction and is not often required to work to its full capacity. That the heart appears to obey the law of "all or nothing" in its contraction as a whole is probably the result of the co-ordination effected by the controlling influences of the sino-auricular node, auriculo-ventricular node and bundle tissue.

Stimulation of the sympathetic nerves of the heart causes augmentation of its beat as well as acceleration. The increased force of the cardiac contraction must be due to the action of the sympathetic in bringing more muscle fibres into activity. Stimulation of the vagus produces varying amounts of decreased force of contraction, and here we have varying numbers of groups of cardiac muscle thrown out of activity.

In auricular flutter and auricular fibrillation the extent of the ventricular contraction may be very variable. An inefficient beat is not necessarily due to little time having elapsed between successive beats, and so having given little opportunity for the ventricle to fill with blood, for it occurs at varying lengths of time after the preceding beat. But if the law of "all or nothing" holds good for the cardiac muscle fibre, the heart can regulate the force of its beat only by utilizing varying numbers of groups of muscle fibres.

The phenomenon is also seen in the "Treppe" or "staircase effect," which is most easily explainable by assuming a gradual calling into activity of an increasing number of groups of cardiac muscle fibres.

We cannot prove that in the ordinary contraction of the heart fluctuation is constantly occurring, but we are of the opinion that it must be assumed. The heart has a great reserve, and it is unlikely that the units which constitute this reserve do not take their part in the routine work of the heart. We assume that there are more muscle fibres in the heart than are at any one time in action when the heart is beating quietly. These muscle fibres take their turn in carrying on the work of the heart, alternating between periods of activity and quiescence. All come into action simultaneously when great effort is necessary, and the occurrence of fluctuation appears to us to be a necessity for the proper maintenance of a sufficient reserve in the heart muscle.

If fluctuation be admitted in the heart, its causation is even more a matter of speculation. The heart differs from voluntary muscle in many ways, and especially in its controlling mechanism. The nodal and bundle tissues of the heart play a part which can in some respects be compared with the myenteric plexus of the alimentary canal. They act as a local controlling mechanism, and are themselves influenced through the central nervous system. It is probably to some local action through the mediation of these tissues that the cause of fluctuation in the heart must be assigned.

It has been mentioned that fluctuation is a phenomenon manifested by the receptors, and this is especially well seen in the study of skin sensation. It has long been known that fatigue of the receptors is readily induced, but that a sensation of heat or cold from a skin surface may last for hours under a continued stimulus. In an investigation carried out in the Clinical Institute, Waterston has found that the heat and cold spots of the skin are constantly appearing and disappearing. The receptors for most forms of skin sensation are situated in the epidermis, and are probably the cells of the deeper layers of this structure. Apparently these receptors are constantly varying between activity and rest. In some pathological conditions the alternation is even more pronounced. The margin, between skin showing normal sensation and skin showing hyperæsthesia, is a very good example of fluctuation. Sir James Mackenzie [10] called attention to the fact that the margin is continually varying. That its cause may be a local one in the receptors is evidenced by the alterations produced in sensation as a result of conditions affecting the epidermis. The application of a mild irritant, for example, to the skin entirely alters the receptors, and through them the resulting sensations. But the fluctuation of a margin of hyperæsthesia usually occurs as the result of some lesion in the spinal cord, and it may be that the phenomena are in this case due to fluctuation in the synapses, and consequently to a variation in the incidence of the afferent nerve impulses to the special columns which carry them to the brain.

Fluctuation is already recognized in the capillaries of skin and muscle. Krogh [8], to whom we owe this discovery, states: "Every capillary must therefore alternately open and close, and in the resting tissue, which is poorly supplied with blood, the position of open capillaries must be constantly changing, with the result that the whole tissue is uniformly irrigated when considered over a period of sufficient length." The capillaries appear to be to some extent controlled by reflex action through the central nervous system, but can be dilated by local axon reflexes and by the action of certain chemical substances in the blood, such as histamine (Dale [4]). The cause of fluctuation in the capillaries is not fully understood, and there is some doubt as to the relative importance of nerve control and direct action by chemical means through the blood-stream. The capillary cells, or cells of Rouget, are contractile, and from the point of view of the capillary cell its period of activity must be that of contraction during which no circulation takes place through it. From the point of view of the tissue the dilated capillary is necessary for activity, and it may well be that the tissue has the local power of bringing about that dilatation by axon reflexes or otherwise.

The alternation of activity and rest of the capillaries of the glomeruli of the frog's kidney has been noticed by Richards [11]. The glomerular capillaries reunite to form an efferent arteriole which usually supplies blood to the capillaries of the convoluted tubules belonging to the same Malpighian body, so that the glomerulus, when inactive, probably renders the rest of the tubule inactive. Richards states that the alternation of activity and rest in the glomerular capillaries is an irregular one, and that the glomeruli act independently of one another. The transition from full activity to complete rest is very rapid, the blood flow stops suddenly, and the glomeruli disappear. Richards draws the inference that a local regulatory mechanism must exist analogous to that shown by Krogh to exist in the capillaries of muscle, and states that the intermittence persists after complete destruction of the whole central nervous system. Here again activity of the kidney requires dilatation of the capillaries, that is to say a state of quiescence of the capillary cell. If Richards' observations are correct, that the alternations take place independently of the central nervous system, some local action either of the nature of an axon reflex or of a direct chemical action on the capillary cell must be postulated.

If fluctuation is a universal property of capillaries an important physiological difference is apparent between those organs which are supplied by capillaries and those supplied by a sinusoidal circulation.

The assumption of fluctuation as of normal occurrence in the capillary circulation appears to be necessary to explain the fact that in conditions where there is a universal dilatation or paralysis of the capillary wall the volume of blood is too small for the maintenance of a proper blood-pressure. Heart failure is not infrequent from this cause: the blood stagnates in the dilated capillaries, and the heart ceases to contract because it is obtaining an insufficient supply of blood.

Histological evidence of fluctuation in the glandular secretions is abundant. The pancreas, when fixed during its activity, presents differences in appearance, especially as regards its cellular content of granules, in different parts of the gland. This we regard as an expression of different stages of activity, and the most likely explanation is that not all parts of the gland are in action at the same time. It cannot be inferred that fluctuation in the secretion of the pancreas is dependent upon the nerve supply, for the main stimulus of pancreatic secretion is a chemical one taken to it by the blood-stream. The pancreas, however, has a nerve supply the action of which is not understood. It is possible that fluctuation in the secretion of the pancreas may be the result of fluctuation in the capillary blood supply to the gland, that the nerves of the pancreas are concerned in the process, and that the mechanism is similar to that described by Krogh in skin and muscle. In glands like the salivary, fluctuation, if present, might be expected to result through the nervous system, for the secretion is a reflex process and must be governed by the laws applicable to nerve impulses set up in receptors and conducted over a reflex arc.

SUMMARY.

The term "fluctuation" is applied to the alternation of periods of full activity and complete rest which appears to be a property of the cell units of many, and possibly of all, living tissues. The possession of this property by the cells which constitute the walls of the capillary blood-vessels has been demonstrated by Krogh, and it has been observed in the glomerular capillaries of the frog's kidney by Richards. Its occurrence in voluntary muscle has been shown by Barbour and Stiles. The condition was noticed many years ago by Mackenzie in the constantly varying borders of areas of hyperæsthesia which are found in the skin in some cases of spinal lesion.

The assumption of a "law of fluctuation" appears to be a necessity in the case of all tissues which are subject to the law of "all or nothing." It is therefore specially applicable to muscle and nerve, the cell units of which, as demonstrated by the work of Keith Lucas, Adrian, and Forbes, are governed by this law.

The law of "all or nothing" demands that each cell unit, when in action, should give its maximal response to any stimulus which is capable of producing a response, there being no gradation in the individual unit between complete activity and complete rest.

Gradation of activity in an organ made up of units subject to the law of "all or nothing" is due to varying numbers of units, or groups of units, being brought into action. The "law of fluctuation" demands an alternation of the units engaged, so that in the performance of a moderate amount of work all parts of the organ participate in turn, first one part and then another taking up the work in rotation. Such a mechanism prevents undue fatigue of the individual units, distributes the work uniformly over the constituent elements of an organ, and provides a reserve of units, all of which can be brought into action simultaneously when the need arises, and have not suffered from long periods of disuse.

Reasons are advanced for the assumption that fluctuation must occur in the receptors and synapses of the reflex arc.

An explanation is offered of the presence of numerous branches on the afferent side of each neurone, and their function is contrasted with that of the branches on the efferent side of the neurone. It is suggested that multiple receptors and synapses are necessary for the economical

use of the non-fatigable nerve fibre. The nerve impulse is initiated by the receptor, and its frequency may be of the utmost importance in the production of the end-result. The branching on the efferent side permits a multiplication of the end-result, and an irradiation in the central nervous system which is limited by the resistance of the synapses met with.

The cause of fluctuation is ascribed to the occurrence of slight fatigue in the receptors and synapses, and possibly in the receptive substance between the efferent neurone and the effector organ. In some cases fluctuation may be ascribable to fluctuation in the capillary circulation. The possibility still remains that fluctuation may be an inherent property of the tissue cell.

Examples are given of fluctuation in nerve, muscle, and glands, and its physiological and clinical importance is emphasized.

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HYSTERICAL PAIN.

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EVEN at this date the term hysterical does not have the exact meaning which is desirable in scientific discussion, and still requires to be defined by everyone making use of the expression. All authorities are agreed that an hysterical symptom is one which does not depend on any demonstrable lesion of any part of the body, and that it is psychogenic in origin. It is over the nature of the psychogenic origin that observers fail to agree. Certain neurologists, such as Babinski [1] and Hurst [7], maintain that the hysterical symptom is nothing but the product of suggestion. The psycho-analytic school declare that the hysterical symptom is always a symbolic manifestation of an underlying psychic complex. We believe that, as a matter of fact, careful inquiry into the onset of every hysterical symptom will demonstrate the presence of a suggestion as a determining factor, but that in the majority, if not in all cases, a connection with some sort of complex can be established.

If expressed in physiological terms it becomes more easy to see how this may be. A suggestion, whether it comes from the patient himself or from his environment, is a pattern of stimuli impinging on the receptors of his nervous system. Sherrington [16] has shown that in accordance with the laws of the selective action of the receptors and the various inhibitions and facilitations established in the nervous system, a certain group of neurones will be activated and modified when a stimulus reaches the body. The exact composition of the group is determined as a result of hereditary dispositions and the conditioning which has taken place through life. Under certain circumstances, depending on the relative strength of the stimulus and the synaptic stability of the nervous system, this group of neurones or engram, to use Semon's term, is so modified as to become a persistent entity more or less "closed," that is, not readily modified by future stimuli. This will be specially liable to occur if the stimulus is persistent over a long period. Of such a nature are the hysterical symptoms which occur as perpetuations of organic injuries. For example, the musculo-spiral nerve is bruised but not divided by an injury in the arm. The result is a temporary paralysis of the extensors of the wrist and thumb. That is to say, a stimulus coming from higher levels which would normally induce activation of these muscles as a constituent part of a motor pattern of behaviour, fails to elicit any response owing to the blocking of conductivity of the nerve. Had the muscles responded and the pattern of behaviour been carried out, their very activity would have provided new stimuli, which would have induced activation of other engrams in a series of associations, whereby thought, feeling and action would result. Theoretically, at any rate, such patterns may be almost limitless in variety. Thus the action of these muscles becomes a small but definite part of the reaction of the whole organism to the environment. But, as has been seen, there is a break in this chain, for conation in respect of these extensor muscles does not occur. This in itself tends to close the whole pattern which requires the action of these muscles, and isolates the engram from activation by efferent impulses from higher, i.e., cortical levels. Some weeks later the nerve has recovered from its bruising, conductivity is resumed and the muscles are capable of contraction. There is no difficulty so far as the peripheral arc level is concerned. The muscles work as individual muscles if they form a link in a spinal reflex which is set off, and react to electricity and so on, but the activation from higher levels is inhibited. The synaptic junctions are no longer permeable under ordinary circumstances, hence "voluntary" movement is impossible. To put it in another way, these particular neurones cannot be activated with others on the cortical level in consciousness, i.e., integrated to form part of a complicated pattern of behaviour or movement as distinguished from a muscular contraction. So hysterical paralysis results.

However, another factor may come in. It may be that this particular paralysis is of advantage to some complex in the patient's mental make-up. Let us make clear what we mean by this somewhat loose statement. First of all what is meant by a complex? A recent discussion on this subject [13] has exposed considerable divergence of opinion, but has disclosed some valuable definitions. Adapting our definition from these we would describe a complex as a persistent but poorly organized or "untidy" system of emotional dispositions about an object, which may or may not be capable of being represented in consciousness, in contrast to a sentiment which is a system well organized and is always capable of being represented in consciousness.

The hysterical symptom within a complex is the result of interaction between poorly organized or dissociated thinking, and poorly organized or dissociated behaviour. This persistence of the complex is important for psychology. Shand [15] speaking of sentiments lays stress on their capacity for persistence and adaptation to different circumstances, as opposed to an emotion which can adapt itself to one kind of situation only. The same is true of the complex, although it can and does grow and decay, and even disappear after a time. The persistence of the complex often determines the duration of an hysterical symptom. The "untidy" organization is important. Pear [12] has laid stress on the unpredictability of behaviour resulting from a complex. In the same way the composition of a complex is unpredictable and it gathers to itself most unexpected patterns, in the form of hysterical symptoms. Shand points out that both sentiments and complexes are not merely associated with a common effect, but are also relevant and subordinate to an end. If these definitions are accepted we can explain more definitely the loose expression we have used above. In view of an end, all patterns of behaviour which subserve that end will tend to become associated with and drawn into the complex, and while the complex is in being that pattern will remain more or less unmodified by stimuli which activate patterns outside the complex. In neurological terms an engram subserving such a pattern of behaviour will not be readily activated by stimuli affecting neurones outside the engram which subserves a complex.

To return to our example: suppose that at the time the nerve is recovering two complexes are struggling for mastery, one representing self-preservation or avoidance of social obligations, and the other representing altruistic behaviour. The continuance of paralysis may be of use to both complexes inasmuch as it is a compromise between the two. Thus activation of the neurones governing movement of the muscles may be inhibited, because stimuli from outside the complex can only with difficulty activate any pattern within it. This accounts for both the stability of the hysterical symptom and the difficulty of cure. Perhaps an example of the use made of an hysterical symptom to solve a conflict between two complexes will make things clearer. A lady was in the throes of a conflict between the complexes representing her religious and social duties on the one hand, and those representing self-indulgence and avoidance of life on the other. So keen had this become that suicidal ideas had arisen in connection with the second complex and caused the most acute distress, such a solution being incompatible with the religious and social complexes. One day she stumbled over a low parapet, fell and bruised her back. The suggestion that she could not move her legs was accepted and at once drawn into the net of her second complex, for as she lay in bed, a self-satisfied invalid, she exclaimed, "How fortunate this is, I can't possibly get to the window to throw myself out." Complex number two had temporarily won the day and number one was momentarily satisfied, and the inhibition of stimuli which would cause the perfectly healthy muscles to act was most pronounced.

It should be noticed that although an hysterical symptom is drawn into the pattern of a complex to begin with, by the time that complex has ceased to be of importance to the patient's personality as a whole, the hysterical symptom may have drawn other sets of ideas into association with it and formed a new complex round itself, which will not be resolved till the hysterical symptom is removed. For example, a man is thrown into a state of extreme terror by being exposed to a shell explosion, and as the result of the disorganization of his muscular control he develops a stammer. The hysterical symptom was drawn into his self-preservation complex while the war was on and served this, but later a new self-depreciation complex in relation to unemployment grows round the stammer and persists until the stammer is removed. This explains the divergent methods of treatment and their varying efficacy. In cases not associated with a well-defined complex, where inhibition is chiefly due to habit and prolonged failure to elicit response, direct persuasion readily elicits a series of stimuli from higher levels which overcome the inhibition, but in other cases some resolution of the complex may be necessary before simple persuasion can operate and open up the passage.

From the above it is evident that our standpoint as regards the hysterical symptom is, that it is the product of suggestion and a well-defined complex, and that these determine the localization and character of the hysterical symptom.

We believe that dissociation from cortical control is characteristic of all forms of hysterical symptoms, and our present purpose is to show that this is particularly prominent in relation to hysterical pain, and to indicate certain lines of treatment depending on this concept.

We would define hysterical pain as a release phenomenon in which, owing to functional dissociation of cortical control, the more primitive sensory system convergent upon the optic thalamus is unmasked and holds sway.

The etiology and nature of hysterical pain are subjects which have received singularly little attention in literature, whether from writers on pain in general or from those who deal with hysteria, yet there is no symptom which is so commonly complained of or so greatly considered by the patient. The great difficulty of this study is that pain is entirely subjective and cannot be estimated or measured objectively. Even the distressing appearance of those who suffer really severe pain, such as tic douloureux, is not so much due to the pain as to the secondary effects of fatigue and sleeplessness. It must not be forgotten, therefore, that the intensity of pain felt does not depend on the violence of the stimulus to the pain receptors. In cases of gross neurological lesion, such as that which produces the syndrome thalamique of Roussy, the threshold of pain is actually raised in the affected area, but the intensity of pain felt when the stimulus does produce activation is enormously increased. But even without such gross lesions pain perception may be modified. As Rivers [14] has shown, pain perception may be altogether suppressed by the activation of some other pattern. An airman, whose arm was broken by a machine-gun bullet, described how he felt no pain whatever until he had landed his machine.

If a patient complains of pain, can we say it is all his imagination, and that he feels no pain? Writers on malingering recognize this difficulty but base their conclusions on factors pointing to demonstrable organic causes of pain. Thus Jones and Llewellyn (11) state that "the expert should not dismiss an alleged pain as imaginary or simulated till he has excluded the possibility of an organic cause." These authors also discuss hysterical pain as being associated with hysterogenic zones and stigmata of hysteria. We are convinced that such criteria are valueless, and that unless one can discover the patient in actual fraud the subjective description of the patient should be accepted as a measure of the pain he actually experiences. In practice of course it is not possible to relieve the ultra-sensitive person from his aches and pains, and we have frequently to tell him to carry on and not make a fuss, but it is as well to recognize that we are falling back on the rigorous principle of natural selection in which the weakest goes perforce to the wall.

Our next inquiry must be as to the nature of pain and how it is perceived. Like other sensations that have reached the stage of organization which we can recognize in man, pain presents two aspects for our investigation—one affective and the other cognitive. The first constitutes the feeling aspect—it has much in common with the primitive type of feeling of unpleasure (*Unlust*), and is often referred to by the word pain. This unpleasure, as Freud [3] and Fechner [2] point out, represents what they call a state of extreme psychical tension or instability, and this is characteristic of phenomena of nervous activity released from cortical control or insufficiently integrated to involve cortical control. For example, the epileptiform convulsion and the various *délires*, the psychopathology of which is described by Janet [10]. Hence, this view of unpleasure probably explains why even in normal people extremes of other sensations present an affective aspect practically indistinguishable from pain, for at these intensities they are no longer wholly subject to cortical control, and there is over-stimulation of affective patterns at the thalamic level.

It seems probable that in certain cases of anxiety neurosis unpleasure associated with ideas and not with sensation is actually perceived as pain. The cognitive aspect of sensation consists of the discrimination of quality and reference in space which is associated with cortical sensory areas. As a matter of fact, pain is more affective and less cognitive in its presentation than other sensations, and in accordance with this Head has found that pain is practically unrepresented on the cortex, and that superficial lesions of the cortex have no effect on the pain sensation. Subcortical lesions do, however, affect it, and the most striking effects are produced in conditions of the thalamic syndrome of Roussy and Dejerine, in which the fibres passing from the thalamus to the cortex are interfered with. Under these conditions affective reactions of all sorts are released from cortical control. Amongst these are the affective reactions of pain which are felt with unusual intensity. As a result of such a lesion, acute pains are present which are persistent, paroxysmal, and often intolerable, yielding to no analgesic treatment. Head [5] makes it clear that these pains are due to stimuli from some part of the afferent tract associated with pain receptors, and that they are due to an affective over-reaction. Along with Holmes he established that there were two independent mechanisms associated with the production of pain—superficial and deep. All impulses capable of generating pain become grouped together in the same path, and whether they arise in the skin or in the deeper structures, they become arranged according to functional similarity. Then, after a longer or shorter course, they pass to the opposite side of the spinal cord, and the tracts so formed run up to the optic thalamus without re-grouping, although there may be one or more relays of cells. There is evidence to show, however, that the grosser forms of pain, such as that produced by excessive pressure, may pass by an alternative route.

The function of the optic thalamus in relation to pain sensation is one of great importance, and Head describes it thus: "The essential organ of the optic thalamus is the centre of consciousness for certain elements of sensation; it responds to all stimuli capable of evoking either pleasure or discomfort or consciousness of a change of state. The feeling tone of somatic or visceral sensation is the product of thalamic activity, and the fact that any sensation is devoid of feeling tone (e.g., posture) shows that the impulses which underlie its production make no thalamic appeal." The thalamus undoubtedly represents the highest level of an older (protopathic) system of sensation, which, as Rivers has shown, has been suppressed by and fused with the more recent cortical system. As Head's experiments showed, the function of this older system is restored earlier after lesion of a peripheral nerve than is that of the newer epicritic system. Under these circumstances the response to pain stimuli is characteristic. The pain seems to radiate from the point of stimulus through the surrounding tissues, and its reference in space is vague and inaccurate, though not abolished.

It should be made clear that perception of pain is due to the reception by the thalamus of stimuli from some part of the afferent pain fibres, whether from the end organs in the pain spots in the skin, or in the deeper structures, or as a result of irritation at the level of the dorsal roots, as occurs in meningeal involvement, or at higher levels. Some misconception seems to arise at times from the expression "pain of central origin," used to describe apparently spontaneous pain occurring in certain lesions of the central nervous system. The most notable example of this is met with in Roussy's syndrome referred to above, but Head has shown that these pains are due to excessive affective response to ordinary stimuli of pain, or even of other sensations such as heat and cold. Some doubtful cases have been described in pontine lesions, and there is Mann's classical case where such pains developed after a lesion of the right half of the bulb. This probably has a similar explanation to those cases described by Holmes [6] in association with injuries to the spinal cord, especially in the cervical region. These he ascribed to lesions of the ventro-lateral columns, insufficient to interfere with conductivity but sufficient to modify the impressions that pass through the affected fibres. The so-called spontaneous pains, in so far as they are independent of peripheral excitations, are probably due to the irritative effects of these lesions on the conducting fibres; and the rarity of these pains probably depends on the infrequency of that type and degree of pathological change that can irritate the fibres and yet not block conduction through them.

As has been said before, the persistence of hysterical pain may be due to the strength of the suggestion, or to the interaction of suggestion with a complex. In either case the pain will be of much the same character, since suggestion is a constant factor. Such suggested pain is usually the sequel of pain due to so-called organic causes, though it may be intensified by becoming the vehicle of expression in consciousness of other affective reactions, and will be of greater or less severity according to the suggestibility of the patient. Suggestions are more readily induced in extrovert or tough-minded persons, and less so in introvert or tender-minded persons, but once the introvert has accepted the suggestion he will tend to brood over it and elaborate it until it becomes a dominant factor in his mind. In both types the readiness with which a person will accept suggestion depends on the inefficiency of integration of his brain patterns, and so pain accepted as a suggestion will not be under proper cortical control.

Hysterical pain may be referred to any part of the body, and may be described in as many different terms as there are qualifications to the word pain. These pains will, however, be affective in character, that is to say their localization will be inexact and their intensity will be out of all proportion to the stimulus arousing them.

It is manifest that it would be profitless to discuss all possible varieties of hysterical pain; all we propose to do is to refer to certain types of pain which present special interest from the point of view of diagnosis, psychopathology or treatment.

Headache.

The only feature common to all forms of headache is pain referred to the head. Certain pains may be described as headache by the patient, e.g., the pain of fibrositis of the scalp above mentioned; but really these are cases with peripheral reference of pain just as much as those cases in which pain is referred to parts of the body remote from the head. Can it be that there is some broad and fundamental distinction between headache and other types of pain?

Hysterical headache is a recognized clinical entity; its protean forms however suggest that description based on situation and type of pain have little or no value.

Behaviour is response of the organism to environment, and as we have already seen, it is modified by the conditioning of pre-existent patterns and their corresponding engrams. Hysterical symptoms represent responses involving engrams modified through the agency of suggestion and complex formation. The complex itself indicates former responses on the social level. Hysterical symptoms then represent responses at the psycho-social level, and one of the most characteristic features of this type of response is some degree of cortical or subcortical dissociation.

The symptoms of organic disease on the other hand represent response of the organism to internal somatic factors, e.g., inflammatory foci, and a prominent sign that pain is of organic origin is that it has peripheral reference. The response of the organism in cases of organic origin is then at a lower level than in hysteria. It may be described as a response at the psycho-physiological level, and as a rule this latter form of response does not involve any dissociation at cortical levels. Hence relatively accurate discrimination of and spatial reference of pain is present. Should the local lesion produce some degree of toxæmia, interference with the highest cortical levels occurs. Such interference may reasonably be presumed to produce a condition akin to cortical dissociation in some degree.

On this basis of dissociation at cortical levels, with consequent release and enhanced thalamic activity, it is possible to find common ground for all headaches, hysterical, toxæmic, or the exhaustion headache of true neurasthenia.

Pains in and around the head associated with organic lesions, e.g., sinusitis, dental abscess or meningitis, are, in early stages at any rate, clearly circumscribed, that is they have peripheral reference. It is only in the later stages when through fatigue or injury to the cortex cerebri, as in the case of meningitis, that diffuse headache results. This is the stage of dissociation. Even at this stage there may be some vague localization of the headache, corresponding to the vague powers of spatial reference possessed by the thalamus.

Possibly in this conception of cortical dissociation lies the explanation of the functional element in painful conditions generally. We are all familiar with the fact that intense intellectual preoccupation may suppress even severe pain. In this connection, however, the direction of interest is of course important and presents certain difficulties. Concentration of attention upon a vague, uncomfortable sensation may enhance its affective intensity, until it is appreciated as intense pain; whereas, concentration upon some extraneous subject results in suppression of the sensation of discomfort. It must be admitted therefore that partial cortical dissociation may in no way prevent the "self as knower" from directing attention either towards or away from the "self as known."

Certain cases of cortical injury, e.g., by gunshot wounds, which have been associated with well-marked pain, indicate clearly the ebb and flow of peripheral pain and headache, according as the patient's attention is directed towards his symptoms or away from them to his environment. In these cases the evidence of some degree of partial cortical decontrol has been unequivocal.

To abolish entirely the power of introspection, cortical decontrol must be practically complete, as in epilepsy, in which case loss of consciousness results.

The after-headache in epilepsy corresponds presumably with the period of gradual return of cortical control. Partial dissociation is indicated by automatic activities, by drowsiness, &c., while the appearance of headache indicates some degree of re-establishment of higher control, since the patient must be able to direct his attention more or less in order to appreciate the headache.

To sum up then, there are no striking features pathognomonic of hysterical headache; but, speaking generally, it is affective in character and vaguely localized, its severity depends largely on the attention it claims and bears no relation to the intensity of the stimulus, if indeed any stimulus can be discovered. In diagnosis the process of exclusion and considerations of probability must be employed. The psychogenic origin is to be found in suggestion and the interaction of the latter with a complex, while the physiological explanation lies in synaptic dissociation at or near cortical levels, which unmasks the primitive sensory mechanisms of the thalamus.

Painful Scars.

Scars healthy in appearance and not associated with any known pathological condition are not infrequently the seat of pain. On examination such scars often present the usual characteristics of protopathic sensibility. In some cases pain is strictly localized within the scar and a small neuroma can be found; but the presence of the neuroma is sufficient to exclude such a case from the category under consideration.

There is a second class of case which may be associated with areas of protopathic sensibility, and liable to be regarded as hysterical.

Nerve trunks caught in scar tissue may cause areas of protopathic sensibility in the region of peripheral distribution of the nerve. For instance, in one case the ilio-hypogastric nerve caught in the scar of a kidney incision caused protopathic discomfort of a very intense kind over the region of the cæcum. This was cured by division of the nerve high up, but not before the patient had been submitted to an abdominal section for colopexy and a further operation of colectomy was threatened. Somewhat late in the day the possibility of hysterical pain was suspected, and before the patient was allowed to undergo the operation for removal of her colon she was referred for examination from the neurological standpoint and the cause of her pain was discovered. Here, then, is an organic condition liable to be mistaken for hysterical pain.

Passing to true cases of hysterical pain in relation to scars we have to consider :—

(1) Cases in which suggestion plays a large part.

(2) Cases of hysterical perpetuation of pain, originally of organic origin.

Both types are presumably due to cortical dissociation and show the characteristics of enhanced thalamic activity. They show their essential similarity in that one method of treatment can cure both, though the first class of case, that in which suggestion plays a large part, is not infrequently quite easily cured by some gross form of counter-suggestion. For instance, an intensely painful scar following an operation for varicose veins was quickly cured by a superficial skin incision under gas, made ostensibly for the division of a sensory nerve, but no nerve was divided at the operation.

The form of treatment which has been shown to be successful in the treatment of both types of cases referred to above is hyperstimulation of the painful skin area involved. Three typical cases in illustration may be referred to briefly :—

(1) A sensitive skin area on the back of the neck originating from an attack of herpes eighteen months previously; the skin looked normal but was the seat of intense protopathic sensibility and prurigo.

(2) A painful area in the palm of the hand, following a gunshot injury at the wrist which involved the median nerve; this patient could not bear the lightest touch in the groove between the thenar eminence and the rest of the palm. The condition had lasted nearly two years from the date of the injury.

(3) A case of painful leg and foot, with an area of special tenderness in the hollow of the instep, which, though not of the same hys-

terical type as the above, since it resulted from a central instead of a peripheral injury, supports our contention of the similarity of hysterical pain in general, inasmuch as the same sort of treatment is of service. This case started with a typical thalamic syndrome following a gunshot wound of head, necessitating a small trephining operation. The early acute symptoms slowly subsided, but four years later the discomfort was so great that the patient was very lame and had developed a talipes varus to avoid contact between this painful area in the sole of the foot and the ground. There had been a transient hemiplegia, but when the patient came under our observation there were no signs of organic paralysis.

These three cases were all submitted to hyperstimulation of the painful skin areas. The rationale of the treatment was carefully explained to each patient before treatment was actually instituted. An explanation on the following lines was usually employed : " At the time you were wounded, or when you were first ill, the nerves of sensation conveyed messages as far as a low level in your brain. At this level sensation is interpreted very vaguely, simply as pain or something unpleasant. The highest levels of your brain, which deal with fine discrimination of all varieties of sensation, were temporarily put out of action. This state of affairs has continued long after physical recovery of the injury has taken place. Because you dread all sensation coming from the affected area, your brain is still involuntarily blocking the stream of sensation. You must now learn to tolerate all forms of maximal sensory stimuli ; by so doing all ordinary forms of stimulation, e.g., contact with the air, with clothes, with the ground, will cease to arouse your attention, much less your fear or dread. When this stage is reached the blocking of sensory impulses to the highest discriminating levels of your brain will have ceased, and once more you will appreciate all sensations at their true value."

We have not found it difficult to get patients to submit to increasing stimulations, provided the treatment is carried out sympathetically and gradually.

The forms of stimulation used have included rubbing, kneading, smacking with the palm of the hand or with leather straps, the faradic brush, catching a cricket ball, skipping or hopping on the tender foot ; also extremes of heat and cold, e.g., metallic contacts and hot water.

Results have been decidedly encouraging. In the case following herpes, the patient, an elderly man who was worn out with loss of sleep, found great relief, and in about fourteen days he was sleeping quite well.

The patient with the tender hand was able to catch a cricket ball, thrown hard at him, by the end of four weeks, and he was also able to enjoy sculling exercise on the river.

The patient with the head injury made considerable improvement over about five weeks.

In all we have treated thirty-eight cases with success by this method.

The crude explanation offered above is pragmatically useful in dealing with patients, but it is no easy matter to find a scientifically satisfactory theory to account for the phenomena. Starting from the idea of dissociation of cortical control unmasking thalamic sensibility in the case of hysterical pain in scars, it is difficult to understand why a few weeks of hyperstimulation can secure a more or less complete return of normal sensation in the affected area.

As a rule all these patients are obsessed with their pain and discomfort, and concentrate a great deal of attention upon them, or rather upon means whereby the dreaded pain may be avoided. Apparently this concentration in itself acts as an inhibition, whereby reassociation between thalamic and cortical levels is prevented. It may be that in this method of treatment we are dealing with phenomena closely akin to what obtains in the process of free association in psycho-analysis. This may be clearer if expressed in neurological terms. Deliberate repression by an "effort of will" means that impressions coming from neurones at lower levels are prevented from activating the most highly integrated neurones. As time goes on it is quite possible that this inhibition may take place at lower levels, cf. Hurst's [8] explanation of the abolition of the blink reflex in hysterical blindness, and in cases of unconscious repression, where inhibition may occur at comparatively low levels in the nervous system. However, in such cases as those under consideration, the inhibition occurs at subcortical levels at lowest, and it may well be that the removal of the effort at repression alone does much to remove the inhibition, and with re-education paths from thalamic to cortical sensory levels again become permeable.

Visceral Pain.

Head has pointed out that visceral pain belongs to the protopathic thalamic system, and in consequence its reference is vague and its intensity extreme. It follows, therefore, that in this region hysterical pain does not differ materially from that produced by organic disease. For this reason differential diagnosis presents great difficulties, and without question this accounts for many surgical operations performed in all good faith for apparently unequivocal symptoms, but which disclose little or nothing abnormal. The only way to guard against such mistakes is the greater exactitude of diagnosis and the education of surgeons to consider mental factors in their patients, for though such operations occasionally do good by suggestion, they more often do incalculable harm. Just as in other parts of the body a definite organic condition is apt to serve as the suggestion which established an hysterical symptom, so in the abdomen it is found that the pain of a duodenal ulcer or an acute appendix will be perpetuated as an hysterical symptom which will persist as a habit pain, or because it is of use to a complex. When this occurs after operation it too often happens that a diagnosis of adhesions is made. Once the patient gets hold of this, the "organic excuse" allows him to rationalize on his hysterical symptom and therefore makes the establishment of proper cortical control more difficult than it would otherwise have been. But it sometimes happens that a second quite unnecessary operation is undertaken to free adhesions, even in the absence of any obstructive symptoms. Needless to say this only makes things worse, and the last state of the patient is worse than the first. Two examples may illustrate how the hysterical symptom may be induced and persist. The first was a man who while in a small tropical station acquired a duodenal ulcer. At the same time he developed a neurosis as a result of various domestic and social maladaptations, which resulted in a marked self-depreciation and dread of going out and mixing with people. He came home and underwent an operation at which the ulcer and all the symptoms except the pain were removed, but for six years he persistently complained of attacks of pain similar to those which he had experienced as a result of his ulcer. On closer investigation it was found that the pains only came on severely when his wife wanted him to go out or social duties called him into the society of strangers. The pain pattern had been drawn into the complex of his self-depreciation, which determined his social behaviour, and whenever this was activated the pain was experienced and proved a useful means whereby this complex controlled the behaviour of the patient.

Another case was that of a boy, who while in France in the line had an attack of acute appendicitis. He had had a good deal of difficulty in sticking it out, and this probably had to do with the fact that after the operation, which was performed in the end of July 1918, the vomiting and pain continued. So violent was this that it was thought that obstructive adhesions had formed, and in the end of August his abdomen was again opened but no abnormality was found. From this time matters went from bad to worse and he was given morphine for the pain and was fed by nutrient enemata. At the beginning of November, at about the time of the Armistice, he was admitted to a Neurological Hospital and in three days was on normal diet and was suffering no pain. All went well until about Christmas, when he received a letter from a girl with whom he had been entangled before he went to France and from whom he thought he was free. This letter gave rise to serious conflict, as he did not wish to tell his parents about this affair and without their help could see no way of escape. At once he started to vomit again and complained of and obviously suffered severe pain. When urged to face the problem and come to a decision he stated that the pain was so bad that he could not possibly think, but the influence gained over the patient by the previous success of psychotherapy made it possible to get him to give his mind to the problem and solve the conflict next day; with this the vomiting and pain disappeared for good. This is an interesting illustration of how the disorganization of cortical control which resulted from the temporary insoluble but quite conscious conflict allowed the activation of the old engram with its thalamic type of response.

In cases of visceral pain then it is impossible to diagnose whether it is hysterical or not from the type of pain, since all such is thalamic in character, and the diagnosis can only be by inference, both negative and positive. That is to say, by the absence of other symptoms and signs which should be present were the lesion organic, and by the recognition of some foregoing suggestion such as would be likely to determine the pain as an hysterical symptom, or of some psychological reason for the persistence of pain.

It may be well to notice a type of pain which is often referred to as hysterical but which is not really so. This is the pain which accompanies muscular contractures which are themselves hysterical. One of us [4] has described a series of such cases which occurred as hysterical complications of "rheumatic" conditions. "In this state the pain which is present is no longer due to inflammation, but to the cramp produced by the muscles which are being held in a state of abnormal tone, and to the stretching of fibrous tissues and of other muscles, as well as to the pressure which is being kept up on abnormal surfaces in the joints." Such pain then is "organic" in character and exhibits accurate reference and discrimination, and although it disappears as a result of psychotherapy it is not itself hysterical in nature.

The diagnosis of hysterical pain can only be reliably established by a process of exclusion, and while an examination for an organic cause should be thorough it should be carried out as rapidly as is consonant with this thoroughness, and with the greatest care to avoid suggestion; for otherwise not only may an hysterical symptom be perpetuated but the subjective affective element in the pain which is experienced may be increased. The old search for hysterical stigmata is futile and misleading, for, as Hurst [9] and others have shown, such stigmata can be produced as fast as they are looked for. The only positive evidence of hysterical pain which can be relied on at all is, if there has been a strong suggestion to determine the pain, and if the presence of the pain may be of such use to a well established complex as to outweigh the unpleasant feeling induced in the personality as a whole.

With regard to treatment little more need be said here. So far as the suggestive influence is concerned it may be removed by counter-suggestion and re-education, and so far as involvement in a complex is concerned this latter must be resolved by the methods now familiar to all workers in this field. The whole object of such treatment, however, must be to re-establish integration on the cortical level, that is to say, in psychological terms, in consciousness, and we have sought to show that hysterical pain like other such symptoms is a dissociation from this level, and that our object must be to restore integration.

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Proceedings of the Section of Neurology of the Royal Society of Medicine.

Meeting held April 12, 1923.

Pathological Findings in the Central Nervous System of a Case of Myasthenia Gravis.

By Sir FREDERICK W. MOTT, and Dr. Y. A. BARRADA.

THE patient joined the Army in August, 1914. His illness began in 1918 with weakness of his lower limbs: a very short walk "did him in completely." There followed progressive weakness of all his limbs but no pain or paræsthesia accompanied this. Two weeks later fluid began to return through his nose, his voice became weak, and chewing food became almost impossible. Major Walshe examined him in July, 1918, and found the masseter and temporal muscles exceedingly feeble. There were marked double facial paresis, and paresis of palate, larynx and pharynx. The whole musculature was very weak and readily fatigued. Sensation and reflexes were normal. Myasthenia gravis was diagnosed. On his way back to England he was reported to be liable to attacks of respiratory failure. In September, according to a report of the Medical Officer of the Maudsley Hospital, the patient had partial ptosis of the right eye, his lips parted, and the smile had the appearance of a sneer. He was unable to wrinkle his forehead, close his eyes firmly, whistle or blow out his cheeks; and he was unable to masticate his food. Speech was good in the morning, but towards evening the muscles of articulation tired and the voice became slurred. The intercostal muscles were also affected. He had diplopia which was not constant in position, his knee-jerks were absent, but there was no loss of sensation. On February 19, 1919, the patient had an attack of dyspnœa which continued until death, which took place the same day.

The post-mortem was performed on the same day; the following changes were found.

The thymus weighed more than 70 grammes, and was completely surrounded by a thick fibrous capsule. Microscopically there was no distinction between its cortex and medulla; the tissue was composed of a mixture of faintly stained epithelioid cells with large vesicular nuclei lying side by side, but a preponderance of lymphocytes varying in density in different places was observable. There were many spaces filled with more or less clear eosin-stained material with some epithelioid cells undergoing colloid degeneration, and a few lymphocytes. These spaces were lined by epithelioid cells arranged in a layer with the long axis perpendicular to the space. Evidence of mitosis could be seen in these epithelioid cells. There were no eosinophil cells, and only a few swollen and degenerated Hassal's corpuscles. The capillary blood-vessels were lined by unbroken endothelium, and contained some lymphocytes.

Muscles.—Numerous foci of lymphocytic infiltration (Buzzard's lymphorrhages), varying in size, were found in the diaphragm, lying between the muscle fibres. The muscle fibres themselves appeared to be normal.

The nerve fibrils and their terminations in the masseter and orbicularis palpebrarum muscles were stained by Dogiel's method with intravitam methylene blue, and appeared to be normal.

Central nervous system.—There was general diminution of the basophil substance throughout the central nervous system. This was most marked in the small and large cells of the thalamus and was associated with vacuolation, eccentric nuclei, invasion by satellite cells and increased neuroglia. Similarly, the third nerve nucleus showed very marked changes, but to a less degree than the thalamus; in the trochlear nucleus they were still less pronounced. The other cranial nerve nuclei as well as the anterior horn cells of the spinal cord showed very little basophil change, although here and there some cells were found with marked chromatolysis, eccentric nuclei and swollen and vacuolated cytoplasm.

With Scharlach and Nile Blue stains, widespread lipoid changes were observed in the cells, and were noted to correspond in their intensity to the amount of chromatolysis, These lipoid granules were also found in the perivascular spaces, which afford a proof of the lipoid change having occurred prior to death. It is noteworthy that the changes observed in the cortex and cerebellum were less pronounced than in the abovementioned regions.

There was general congestion of blood-vessels, but no hæmorrhages. No lymphorrhages were found anywhere.

Unfortunately no other tissues were obtainable for examination.

As regards the pathogenesis of myasthenia gravis, the view is gaining ground that it is primarily due to some form of autotoxin resulting from a disturbance of the internal secretions or disordered metabolism, which exerts a deleterious effect on the functions of the muscles. An exotoxin seems to be capable of exerting similar influence, since myasthenia has been observed to follow infectious diseases and such poisons as barium salts, chlorine gas, war gas, &c. The fact that in the myasthenic electrical reaction the muscle reacts well to galvanism after complete exhaustion to faradism, suggests that the primary seat of fatigue is at least not limited to the muscle. Further, there is not sufficient evidence, on pathological grounds, to show that the muscles or nerves are directly responsible for the phenomena of fatigue exhibited by the patients in voluntary movements. Considering these facts, and that cellular changes in the nervous system have been described by Kalischer, Widal, Marinesco, Murri, Guthrie, Leclerc and Savornat, it is quite possible that the changes in the central nervous system found in this case may be correlated with the manifestations of myasthenia.

DISCUSSION.

Dr. GORDON HOLMES stated that though he could not doubt the correctness of the observations made by the authors, he could not accept them as explaining the disease from either the pathological or clinical standpoint. In the first place it was surprising that the changes as were here described have not been detected previously in the large number of cases of myasthenia gravis which had been examined by competent neuro-pathologists. In the second place he did not see how the clinical phenomena of the disease, and especially the localized muscular disturbances which were present in many cases, could be explained by them. He pointed out that single muscles or irregular groups of muscles only might show prominent changes, such as orbicularis oculi or oris, or as in a case at present under his care the triceps, and asked how this localization could be accounted for by such a diffuse and general affection of he central nervous system, for cerebral affections lead to disturbances of movement and not of the functions of individual muscles. It was also striking that despite such changes the symptoms were practically limited to the motor system. It seemed to him that all the pathological findings which had accumulated during the last twenty years, since Weigert originally pointed out the association of myasthenic symptoms with tumours, hyperplasias or persistence of the thymus gland, indicated that disturbances of the normal functions of this gland must play an important part in the pathogenesis of the symptoms. In six of the eight cases which he had himself examined by autopsy there were either tumours or enlargements of the thymus. It seemed to him that it was only from further studies of the physiology of the thymus that we could expect much light on the pathology of this disease.

Dr. WALSHE asked how Sir Frederick Mott would explain the absence of mental and other symptoms if the lesions of the central nervous system which he and Dr. Barrada had described were of pathological significance. He felt convinced that the paper threw no light on the nature of myasthenia gravis.

Dr. GREENFIELD also insisted on the importance and frequency of tumours and the enlargements of the thymus: negative observations seemed to him of little value unless the mediastinum was carefully and systematically searched, since thymus tissue could be easily overlooked in the fat of this region. In three cases on which he had recently performed autopsies the thymus was persistent, and though not much enlarged each consisted of glandular tissue and was obviously functional. Microscopical examination revealed proliferation of the epithelioid cells, which in places seemed to be going on to the formation of Hassal's corpuscles. It is difficult, however, to say whether these changes in the thymus are primary, or secondary to the disease of some of the other endocrine glands. He has failed to find any lesions in the parathyroids that could support Chvostek's hypothesis. In one of his cases there was certainly no excess of lipoid, such as has been described by Mott and Barrada, in the nerve cells.

Dr. SYMONDS referred to some ergographic observations he had recently made, which could be most easily interpreted by assuming a lesion in the nervous mechanisms of movement. First, he determined the strength of a faradic current necessary to produce a brisk response of a muscle; then he exhausted the muscle by voluntary contraction, and when it no longer contracted to voluntary stimuli he found that he could immediately obtain an undiminished response to the same strength of faradic current. He also referred to the pains and other sensory symptoms that are occasionally observed in the disease. He described a case which had recently died under his care, in which, in addition to weakness of the muscles of the jaw and of the external ocular muscles, clonic twitchings of the right limbs and disturbances of speech occurred. There was also loss of taste. This patient had very severe dental sepsis and he suggested that toxins carried from the mouth to the brain may have induced the changes which excited symptoms of the disease. Post-mortem examination revealed an enlargement of the thymus and cellular infiltration of the muscles.

Dr. BIRLEY said that it seemed to him that there was no evidence that the case referred to by Dr. Symonds was one of myasthenia gravis; it was much more probable that the so-called myasthenic symptoms were due to a neuritis of the cranial nerves.

Dr. FEILING stated that he discovered no enlargement or persistence of the thymus in three cases on which he had made post-mortem examinations, though the effect of pregnancy on the disease suggested that some endocrine disturbance played a part in it at least.

Sir FREDERICK MOTT in reply pointed out that he did not regard the changes which he and Dr. Barrada had discovered in the central nervous system as definitely proven to be the cause of the disease, though they were certainly significant. He could not deny that the frequent enlargement of the thymus was important, but its exact cause was still a matter of doubt ; it may be only the effect of a general endocrine disturbance.

CLINICAL MEETING HELD MAY 10, 1923.

By Dr. A. FEILING.

(1) *Case of (?) Progressive Double Athetosis.*

A boy, now aged 9, was a normal child at birth, and so continued until August, 1919, when, as the result of a street accident, he had his right foot amputated. After recovery, and when he began to use crutches, involuntary movements were noticed in both arms. Later these movements affected the legs as well. Three years ago dribbling from the mouth began, shortly followed by a progressive loss of speech. Until about eighteen months ago he was able to swallow well, but in the last year spasmodic movements of the jaws have seriously interfered with feeding. The mental faculties have not suffered. He has had measles, chicken-pox and erysipelas. No history of any nervous or mental disease in the family ; there are three other children alive and well ; one child died of pneumonia, and there was one miscarriage three months after marriage.

On examination the child is undersized. He is now quite unable to speak, but he can indicate by signs what he means and is perfectly intelligent, though the mental state is retarded for his years. Pupils and optic discs normal. No paralysis of the ocular muscles or of the face. Constant spasm of the jaws leading to marked grinding of the teeth and interfering with feeding and mastication. The tongue can hardly be protruded at all, and, when it is, is deviated to the left. Swallowing is very difficult and food sticks in the throat.

The arms, and especially the left, are the seat of involuntary movements. These take place at all the joints, but are most marked at the shoulders. They are more of the type of athetosis than anything else. There is no actual paralysis. There is not much alteration in the muscular tone, though, perhaps, some hypertonus is present. The arm-jerks are present. Similar movements affect the legs, but the right more severely. The knee-jerks and the left ankle-jerk are active. The left plantar response is somewhat doubtful, probably flexor. No loss of sensation has been found. He is quite unable to stand even with assistance, and a peg leg, and now cannot sit up unaided.

One year ago the Wassermann reaction in the blood was feebly positive, but the cerebrospinal fluid was quite normal. The Wassermann in the blood of the mother is negative. He was treated a year ago with antisyphilitic remedies, mercury and iodide and intramuscular injections of glucarsenol. Some improvement took place, but recently there has been a slow deterioration, especially in the power of swallowing.

(2) *Case of Chronic Mercurial Poisoning.*

By Dr. E. A. CARMICHAEL.

Patient, a male, A. S., aged 51, thermometer maker.

History: Eighteen months ago teeth became black and loose. Twelve months ago gums were painful. Three months ago salivation and unsteadiness of hands with "trembling" of legs. Two months ago difficulty in going upstairs, followed later by weakness in wrists. Seven weeks ago bad occipital headaches and aching in knees and wrist. Looseness of bowels of indefinite duration. During the last three months memory has been very bad and speech slurred. No history of stabbing pains, vomiting, delusions or obnoxious taste.

On admission: Skin of body, and especially of face, dirty sallow colour. Teeth few in number, black, loose with retracted gums. Tongue raw looking. Arteries slightly thickened. Fundi normal. Pupils equal, no ocular abnormalities. Lower jaw trembling as if silently mumbling. In the hands and legs similar irregular tremor. Grasp poor, extensors of wrist weak. Plantar flexion of both ankles weak. Reflexes normal. Diminution to pinprick and cotton wool of glove distribution on arms, over legs and on the lower trunk. Blood count and picture normal. Gastric contents showed diminution of free HCl. Cerebro-spinal fluid and blood normal.

The patient has improved considerably since admission.

(3) *Case of Muscular Atrophy of the "Peroneal" type apparently commencing in, and confined for some time to, the right hand.*

By Dr. C. P. SYMONDS.

The patient, Mrs. C., aged 32, belongs to a family in which I have found nine members affected by the disease in two generations. She belongs to the senior generation, and her father is also stated to have suffered from the disease. Her sister, Mrs. B., aged 38; her niece, Miss B., aged 15; and her nephew, Mr. William C., aged 17, are presented as typical cases of peroneal muscular atrophy.

The present patient, Mrs. C., states that she has noticed from childhood that the fourth and fifth fingers of her right hand would not straighten out properly. She has never been seriously inconvenienced by weakness of either hand. She was at school till the age of 14, then in domestic service for six years, married at 23, and has two children aged 8 years and 2 months, whom I have seen, and who appear in every respect normal. The deformity of the right hand was recognized by the family from childhood. She states that she has suffered from no illnesses except occasional headaches, and that she has noticed nothing wrong with her feet.

Her general condition is good, and her mentality normal. The right hand shows wasting of the intrinsic muscles of moderate degree. This is essentially of the ulnar type. The intrinsic muscles of the thumb are slightly, if at all, affected. The hand is deeply hollowed, the hypothenar eminence is lacking, all the palmar and dorsal interossei are wasted and weak, the wasting and weakness roughly corresponding. The left hand is relatively normal. Both feet show pes cavus with claw toes. This is of moderate degree and more pronounced on the right than on the left. Power in the feet and legs is good on the whole, though dorsiflexion is somewhat weak on the right. When examined a month ago fibrillary twitching was noted in the peronei of both legs, being more noticeable on the right. Sensation to cotton-wool and pin-prick is normal, but sense of position is slightly impaired on the toes. Sensibility to the vibrating tuning-fork estimated quantitatively appears diminished both in legs and arms. The ankle-jerks could not be obtained; knee-jerks sluggish, obtained only with reinforcement; left triceps-jerks greater than right; supinator-jerks not obtained; abdominal reflexes present and equal, and the plantars indefinite.

DISCUSSION.

Dr. STANLEY BARNES referred to a series of cases in which he had found a somewhat similar type of myopathy. In this series there was a strong inheritance, the disease could be traced back in the family as far as 1804. One of the most unusual features was the degree of variation at different periods of life, so that some of the cases appeared at one stage to be of the true hypertrophic type, at another of the juvenile type, and in one case at a late stage it might have been thought that the patient was suffering from the distal type of myopathy. He expressed his interest in these cases, and hoped it would be possible to publish both series at the same time.

Dr. F. J. NATTRASS said he had recently seen two cases of this disease in brothers, both of whom had double drop-foot due to wasting and weakness of the anterior tibial groups of muscles, but in both the peronei still retained good voluntary power. Strong faradism failed to elicit any response in the tibiales antici, but the response of these muscles to galvanism was almost as brisk as normal. The peronei contracted well to faradism.

(4) *Case of "Juvenile" Tabo-paresis.*

By Dr. C. WORSTER-DROUGHT.

R. P. B., MALE, aged 26. No history of any illness of importance before onset of present disorder, Was up to the average standard at school; on leaving, worked as a "light porter" in Government service until his mobilization with Territorial Forces in August, 1914. In January, 1917, he appears to have had a "seizure," and, as a result, was discharged from the Army in May, 1917. He returned to his civil employment and continued until 1919, when increasing mental deterioration and the fact that "he was always falling asleep" led to his dismissal.

Present condition: Invariably cheerful and self-satisfied; childish and inane, but usually answers questions fairly rationally; inclined to be grandiose in his ideas with some degree of confusion; memory for past events very poor and orientation fairly good. No delusions. Both pupils irregular in outline with no reaction to light, direct or consensual. Optic discs somewhat pale. Hutchinsonian teeth. All arm-jerks brisk, knee- and ankle-jerks absent. Ulnar nerve and tendo-Achillis analgesic. Frequent urinary incontinence. Some unsteadiness of gait and Rombergism, but not marked. Wassermann reaction positive in the blood. Cerebro-spinal fluid (last examination) 272 lymphocytes per cubic millimetre, globulin and Wassermann reactions positive, colloidal gold curve of "paretic" type.

Under observation and treatment with novarsenobillon intravenously and mercury cream intramuscularly at intervals during the past four years, patient has shown very little change, excepting for a steady increase in the cell content of the cerebro-spinal fluid, from 88 cells to 272 cells per cubic millimetre.

(5) *Case of Juvenile General Paralysis of the Insane.*

By Dr. C. WORSTER-DROUGHT.

C. M. D., MALE, aged 22. Patient left school in Standard VI at the age of 13, having had no illnesses except attacks of bronchial catarrh each winter. When he was 14 years old he began to "stammer," but was able to carry on with his work until he was 18 (four years ago); he then had a "fit," and was unconscious for twelve hours. Since that time he has steadily deteriorated, both mentally and physically. His father died sixteen years ago (aged 40) from pneumonia, while his only brother, aged 15, has interstitial keratitis. His mother is alive and well.

Present condition: Mentally dull and stupid, and easily amused, but occasionally he answers questions fairly intelligently. Both pupils inactive to light, direct and consensual: optic discs not unduly pale. Arm-jerks brisk and equal, abdominals brisk and equal, knee-jerks both present, ankle-jerks unobtainable, plantar reflexes flexor. No ulnar nor tendo-Achillis analgesia. Gait uncertain and unsteady but no Rombergism. Wassermann reaction positive in the blood. Cerebro-spinal fluid (last examination) 82 lymphocytes per cubic millimetre; globulin and Wassermann reactions positive.

During the past three years he has been treated with courses of novarsenobillon intravenously and mercury cream intramuscularly; the only changes are increasing tendency towards dementia and loss of ankle-jerks.

(6) *Case of Huntington's Chorea.*

By Dr. C. WORSTER-DROUGHT.

J. T., MALE, aged 45, complains that he "cannot keep still," the continual movements resulting in insomnia. The condition developed in 1917 while the patient was serving in France, but he was able to continue in the Army until 1919. In spite of a variety of forms of treatment the movements persist unchanged.

Present condition: If observed he is seen from time to time to exhibit jerky movements of the head and limbs; the neck is jerked backwards, the back straightened, and the head then falls forwards, and the back becomes bowed. The hands may be thrown to one side with the whole arm sweeping outwards; while sitting he has found that his feet are continually shuffling owing to the leg movements. All the movements are loose, jerky, and show a wide excursion. It is understood that his wife is "always grumbling because he moves about so much in his sleep." Under hypnosis the movements continue, but are less pronounced. Mentally, he is irritable, depressed, and his memory for past events very poor. Speech is indistinct, and somewhat grunting in character, and is often accompanied by lateral movements of the head. The pupils, fundi and other cranial nerves show no abnormality, the knee- and ankle-jerks are active, and the plantar reflexes flexor. Wassermann reaction is negative in the blood. Cerebro-spinal fluid: two cells per cubic millimetre; Wassermann negative; globulin slight increase; colloidal gold reaction "luetic" curve (0.1.1.1.1.2.2.1.1.0).

Family history: Nothing of importance can be traced. He has been married six years and has no children. His mother died when he was 14 (thirty years ago)—of what disease he does not know—and his father as the result of an accident twenty years ago. He has a brother, three years older than himself, and a sister three years younger, both alive and well.

(7) *Casé of Quadriplegia with Traumatic Spondylitis.*

By Dr. DOUGLAS MCALPINE.

M. D., FEMALE, aged 42, was well until February, 1921, when she fell into an area. She immediately lost consciousness. Later she found she could not move her head or any of her limbs. She had retention of urine. At end of one week power began to return in left arm, and gradually the other limbs recovered, but a general weakness has remained, this being most marked in her right arm. Since the accident she has suffered from shooting pains across the back of neck and down both arms. She has shown progressive improvement whilst under observation.

Examination shows nothing abnormal in the cranial nerves. No localized wasting in shoulder or arm muscles. No sensory disturbance in limbs or trunk. Moderate loss of power in both arms, in the right more than the left. Tone in right arm is increased in triceps and flexors of the wrist. Posture of right arm when walking is one of extension at the elbow, pronation of the forearm, flexion at the wrist. No material change in tone or posture in left arm. Tone in the lower limbs is slightly increased in extensors, but power is quite good. Deep reflexes are much exaggerated in arms and legs, but more so on right side. Right plantar response is extensor, while left is equivocal.

X-ray examination shows bony outgrowth from third, fourth, fifth and sixth cervical vertebræ.

(8) *Case of Syringomyelia with Pain of Central Origin.*

By Dr. A. G. DUNCAN.

W. M., MALE, aged 37. Fifteen months ago he first noticed a weakness in his left arm, which has gradually progressed. Pain was also experienced in left arm, and later in left upper chest and left side of the face and this has persisted.

Examination shows hyperæsthesia to cotton wool and pinprick, with partial loss to heat and cold in distribution of left fifth cranial nerve. In addition there is moderate loss to all forms of sensation on left side of neck, left arm and left side of the trunk, extending down to the level of eighth dorsal segment. The loss of postural sensibility is very marked in left arm. Nystagmus present. No involvement of other cranial nerves. No muscular atrophy left arm. Deep reflexes more active on left side, and left plantar response is extensor in type. There is no loss of sensation in left leg or on trunk, or in the limbs on right side.

(9) *Case of Right Frontal Tumour; Cracked-pot Percussion Note over Right Frontal Bone; Left Palmar Reflex.*

By Dr. GEORGE RIDDOCH, and Dr. BRAIN.

W. G., aged 8, Hebrew boy, left-handed and a twin, was noticed six months ago to be weak in the left hand: this has become progressively weaker. He has complained of headaches, beginning in the right temporal regions, for four months, and has vomited every few days for the same period. His face was noticed to be "on one side" two months ago; and there is a history of occasional stammering and some indefinite visual impairment.

On examination on February 20, 1923, there was a visible boss on the skull in the right temporal region, divided by the right fronto-parietal suture. On percussion a cracked-pot sound could be elicited over the right frontal bone while the left yielded a boxy note. The fundi showed blurring of the edges of both discs with one diopter of swelling in the right. There was a left hemiparesis, the weakness affecting the facial movements most, the arm to a less extent, and the leg only slightly. Sensation was normal.

A fortnight later small clonic movements were observed in his left face and arm, and in his right leg.

Palmar reflex: It was noticeable that objects placed in the left hand were the more strongly clenched the more one attempted to pull them away. This reaction can still be obtained, and is evoked especially by moving contact from the flexor surface of the fingers and especially of the first finger and thumb. The reaction is entirely involuntary, for the patient obviously makes strong efforts to relax his grasp. He is usually unable to extend his fingers, but the reflex can be well evoked even when spasm of the fingers is largely eliminated by passive flexion of the wrist.

At the present time there is some loss of postural sensibility in the fingers of his left hand. Tactile discrimination, localization and sensibility are also defective in the left upper limb. There is now some secondary atrophy of both optic discs.

Meeting held June 14, 1923.

Hysterical Fits, with some Reference to their Treatment.

By Dr. L. R. Yealland.

This paper, which was based on observations made in one hundred cases of hysterical fits, over a period varying from two to seven years, dealt with the subject more from a physical than from a psychological aspect. The author pointed out that victims of hysterical fits can be made to reproduce a seizure by simple methods. In some cases a command to demonstrate the attack is all that is necessary ; in others, considerable persuasion is needed. The patient's response to reproduce a seizure to order is considered to be of some diagnostic value, and it is employed as a suggestive factor in the plan of treatment he adopts, which consists in demonstrating to the patient during the seizure so reproduced that consciousness is retained throughout the attack.

The following classification of types of seizures was suggested: (1) An apparent momentary loss of consciousness. (2) A state of apparent coma lasting for hours in which the pulse and respiration rates are normal. (3) A pseudo-tonic convulsion. (4) A pseudo-clonic convulsion. (5) A convulsion beginning in the pseudo-tonic contraction and followed by a pseudo-clonic contraction. (6) Hystero-epilepsy. (7) Attacks of uncontrollable laughing or crying in which large quantities of urine are passed. (8) Other violent movements expressed in attempts to injure himself or those who attempt to restrain the patient by holding him down. (9) Attacks of staggering.

Illustration of each type of case was given, together with the treatment employed, and it would appear therefrom that the method of application varies somewhat in each case. It is one of suggestion and re-education. The percentage of recoveries from recurrence of attacks was given as sixty. Types 3, 6 and 7 were more difficult to treat, but even in them a marked reduction in the number of seizures was noted.

Discussion.

The paper was discussed by Drs. Reynell, Patrick and Harris, who agreed that such methods as were advocated in it have often a considerable pragmatic value. Surprise was expressed that a larger proportion of permanent cures had not been obtained by the author.

NOTICES OF RECENT PUBLICATIONS.

Die Lehre vom Tonus und der Bewegung, zugleich systematische Untersuchungen zur Klinik, Physiologie, Pathologie und Pathogenese der Paralysis Agitans. Von F. H. LEWY. S. 673, mit 569 zum Teil farbigen Abbildungen und 8 Tabellen. Berlin: J. Springer. 1923. Price 40s.

It is mainly to the study of paralysis agitans that this large monograph is devoted, but in his effort to be as complete and comprehensive as possible the author has extended his work to many cognate subjects, as tonus and its chemico-physical basis, the physiology of the co-ordination and synthesis of movement, the development and structure of the corpus striatum, and the anatomy and physiology of the vegetative system. All these chapters are well worth reading, though some of them contain little new or striking in the matter of observation or in the explanation of function.

It is, however, those sections on the clinical and pathological aspects of Parkinson's disease that give the book its undoubted value. His observations on the pathology of the disease alone are based on the histological investigation of the central nervous system in sixty cases.

In the first chapter interest falls mainly on the careful study of the vegetative and psychical disturbances of paralysis agitans, and the conclusion that this disease is to be regarded as a pathological form of premature senility in which, however, the lesion falls on the centres of involuntary mobility and on the vegetative nervous system, rather than on the cortex.

There follows in the second chapter a lengthy analysis of movement by direct and indirect muscle tracings, and by the simultaneous recording of electrical changes in the agonists and antagonists by means of two string galvanometers, in various nervous disorders as well as in paralysis agitans. The special form and the significance of the various types of curves obtained in the latter disease are fully considered, and important conclusions as to the nature of the disturbances of nervous functions that they indicate are discussed.

The anatomy of the disease is also dealt with in a very complete and thorough manner. Structural changes are described in most parts of the nervous system, in the cerebral cortex where the frontal and temporal lobes suffer most, in the cerebellum and in the brain-stem, but the most essential are those that exist in the corpus striatum where cellular, interstitial and vascular changes occur more or less independently of one another. All these lesions are of an analogous nature of those found in senile and presenile degeneration, and their anatomical localization is to be explained, according to the author, partly by the peculiar mode of distribution of the blood-vessels in the affected region, and partly by a primary affection of the liver, and perhaps, too, of some of the ductless glands, as the thyroid, which makes the corpus striatum and related parts of the nervous system more vulnerable to various pathological agents than they usually are.

Though certain of the author's conclusions may not be generally accepted, and though some of the arguments on which he bases them may become subjects of controversy, the volume must be regarded as a valuable contribution to the study of subjects on which much ignorance still exists. The manner in which the volume is published, and especially the reproduction of the numerous illustrations, deserves the highest praise.

Der amyostatische Symptomenkomplex. KlinischeUntersuchungen unter Berücksichtigung allgemein pathologischer Fragen. Von Dr. A. BOSTROEM. S. 205 mit 12 Textabbildungen. Berlin: J. Springer. 1922. Price 7s. 6d.

The title of this monograph is the term introduced originally by Strümpel to include disturbances of fixation of parts of the body owing to errors in the time or degree of the innervation of the muscles that subserve it, or to irregularities in their combinations. The clinical conditions which the author includes in it and describes here are idiopathic and symptomatic athetosis and chorea, progressive lenticular degeneration, pseudo-sclerosis and paralysis agitans, or rather Parkinsonism as a result of various structural affections of the brain. The clinical features of each of these conditions is carefully described and analysed, and in many instances are illustrated by the record of cases, especially by such as bring out special features or symptoms. The pathology of each is also discussed, especially in relation to the pathogenesis of the essential symptoms. The book is compact and readable, and will undoubtedly be of service in the study of these interesting diseases.

Die Lumbalpunktion. Dr. MARTIN PAPPENHEIM. Wien, Leipzig, München. Rikola Verlag. 1922. Pp. 184.

Books on the cerebrospinal fluid written by those familiar with the subject are still few, and therefore welcome. Dr. Pappenheim's book makes no pretence to open new ground, or even to cover the whole of the subject, but it is obviously written from personal experience and, so far as it goes, is a trustworthy guide to the examination of the cerebrospinal fluid. It is essentially a book of methods, and is more adapted to the needs of the laboratory worker than to those of the clinician. It deals particularly with the more chronic forms of nervous disease, and with the many special methods which have been devised for the diagnosis of the various syphilitic affections of the nervous system. Nearly ninety pages are occupied in the details of the examinations for cells, albumen and globulin, and with the colloidal gold and mastic, Wassermann, Sachs-Georgi, and hæmolysin reactions. At the end of this we find that the differential diagnosis of general paralysis from other syphilitic diseases cannot be made on the results of any of these tests, either singly or in combination, but only on the alterations which take place in the reactions as the result of treatment. This conclusion is in agreement with the views of most modern authorities. The twenty pages on the diagnostic value of lumbar puncture are somewhat discursive, and many diseases are only incidentally mentioned. We miss a clear statement of the changes found in the cerebrospinal fluid in each disease such as is given, for example, by Eskuchen. In fact, Pappenheim's book, either as a work of reference or as a laboratory handbook, cannot be compared with that of Eskuchen. It contains practically nothing new, and omits much valuable material that is given by the older books. It is, however, much shorter and more easily read. The bibliography is well arranged, and there is a good index.

The Form and Functions of the Central Nervous System; An Introduction to the Study of Nervous Diseases. By FREDERICK TILNEY and HENRY ALSOP RILEY. Second Edition. Pp. 1,019, with 591 figures, 56 of which are coloured. London: H. K. Lewis and Co. 1923. Price £2 12s. 6d.

The first edition of this book was reviewed in a previous volume of this Journal (1921, **44**, 90). The present edition is merely a reprint in which some typographical and a few other errors have been corrected. The authors assert that owing to the short time intervening since its first appearance, no radical changes in the text or illustrations are required, but it is none the less regrettable that some of those defects which were pointed out in the previous review, especially the absence of reference to other authorities on controversial points and the use of terms not generally accepted, should have remained unchanged.

Brain Abscess. By WELLS P. EAGLETON, M.D. Pp. 280. New York: The Macmillan Company. 1922. Price 31s. 6d.

This book, written chiefly from the standpoint of the otologist, consists of some 280 pages, of which number about a quarter are occupied with a review of a very large number of cases taken from the literature. The main part of the book, however, is based upon the author's personal experience of some fifty cases of abscess of the brain, and contains a good deal of interesting information. There are sections dealing with the surgical technique of intracranial operations, with the protective mechanism of the brain, and with the pathology and diagnosis of cerebral abscess. The author's method of dealing with such abscesses is given in much detail, but it is somewhat surprising to find no mention of enucleation of the entire abscess with its capsule.

Der Selbstmord. Dr. R. Weichbrodt. Aus: Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten. Heft 22, S. 44. Berlin: S. Karger. 1923.

This small monograph is an interesting study on the problem of suicide from the historical, religious, sociological, philosophical and psychiatrical points of view. Statistics show that there are a greater number of suicides in large towns than in country districts; and that it is more common amongst the more educated classes, especially among those subjected to the stress of modern business. In the nineteenth century suicide was much more common in Europe in men than in women, in the proportion of four to one, but in the last few decades the proportion of female suicides has increased, especially in districts in which women have entered business and competition for livelihood. Religion has apparently little influence in checking suicide, in fact certain religions of the East and some of the American and African religions look upon suicide as a duty. The curve of suicide rises each spring, especially in the months of May and June, in every country.

Esquirol regarded suicide as invariably an act the result of psychopathic disturbances, but recently observers have paid more attention to external factors, as financial distress, threatened punishment, loss of friends, &c. Though these are undoubtedly important it is interesting that in many families there seems to be a hereditary tendency to suicide. Only a small proportion, forty to 1,400 suicides, of which a record has been kept in Berlin and Frankfort, have been previously confined in institutions owing to mental aberrations; among the insane the danger is greater at the beginning or end of the melancholic attack.

The only prophylactic measures that the author can suggest are careful education of psychopathic individuals, and confinement to institutions as soon as any signs of mental aberration appear.

Psychology and Morals: An Analysis of Character. By J. A. Hadfield. Pp. 186. London: Methuen. 1923. 6s. net.

In the doubtful probability of man sacrificing the heritage that has been bequeathed to him by the great religious and moral systems of history, the change will take place only after long and painful struggles, compromises, and re-interpretations.

The book before us is an attempt to seize the most favourable moment for the development of the new psychology initiated by Freud and Jung. While accepting the hypotheses of the Freudian psychology for all working purposes, the author tempers the wind to the endurance of the shorn lamb by making a number of concessions to current moral ideas, in order that broad principles of the psycho-analytic position may be accepted without demur. But this does not weaken the force of the book, which is in the nature of a guide to the perplexed layman in his way through the labyrinth of new and somewhat terrifying ideas.

After an enunciation of the principles, Dr. Hadfield discusses the vexing problem of the will rather fully, for on this fulcrum the whole of the moral personality revolves. Dogmatism on this topic is unfortunately necessary in the interest of morality, but it leads to metaphysical difficulties. From this the author goes on to discuss the idealism which can only succeed if it springs from a unified personality in which all impulses are in equilibrium, and serves the moral ends of the individual. Knowledge of the self is necessary before the individual can achieve moral ends which will be in complete harmony with an integrated instinct and emotion-driven system. Psychological analysis alone will achieve this end, and by so doing will bring into harmony the impulses derived from lower strata of our natures.

The book bristles with difficulties born of the attempt to explain the lowest in terms of the highest, with the result that many of its dogmatic assertions would not bear investigation in the light of anthropology, or even in the light of a dispassionate study of the history of morals.

Behaviourism and Psychology. By A. A. ROBACK. University Bookstore, Harvard, U.S.A. 1923.

In the flood of literature from the United States on the subject of Behaviourism, Dr. Roback's book comes as a welcome and vigorous current in the reverse direction. It is an attempt on the broadest possible grounds to reassert the claims of psychology as an independent science; it is not, however, written in an apologetic strain but as though the author saw in attack the best method of defence.

The first part is historical, and traces the origin of the behaviouristic attitude in the work of Hobbes and Comte, and, in our own time, in the neo-realism foreshadowed in William James and fully developed by Dewey, Holt, Watson and others. The author's main objection on biological grounds is that it fails to give an adequate explanation of memory, and secondly, in all experimental investigations, however rigidly introspection may be ruled out, there must be "an injection of the experimenter's own introspection into the interpretation of the data."

In the second section he disposes of the behaviouristic claim to have ousted psychology from its position of lawgiver to the organic life; he does not, however, rest satisfied with his victorious assault but carries the battle on into the fields of ethics, jurisprudence, religion and sociology. "Are these studies possible in the light of Behaviourism?" he asks. Once having established the right of psychology to throw a light on organic life, it appears to follow logically that behaviourism will not apply to the more complex forms of activity.

The book, however, fails to do sufficient justice to the methodological value of behaviourism as an instrument of research. Although one may learn much from the observation of movements as response to stimuli, the significance of such activities is only to be understood by an interpretation of them in terms of ends and purposes. Purpose, however, is a category that has no application to mechanism, and thoroughgoing behaviourism is mechanistic. No sooner is this category admitted than the laws of psychology, as apart from physiology, are *ipso facto* established as existing, although they may not be fully understood. With this established, psychology stands alone as an independent method of investigation and behaviourism takes its rightful place as a method also—a bridge between physiological concepts and mental concepts, and not, as it falsely claimed to be, a complete science and philosophy of the organism.

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Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd. St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

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EDITOR.

[OCTOBER, 1923.

BRAIN.

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THE PATHOLOGY OF THE PARKINSONIAN SYNDROME FOLLOWING ENCEPHALITIS LETHARGICA, WITH A NOTE ON THE OCCURRENCE OF CALCIFICATION IN THIS DISEASE.

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I.—HISTORICAL REVIEW.
II.—ACCOUNT OF HISTOLOGICAL FINDINGS IN TWO CASES.
III.—RELATIONSHIP OF HISTOLOGICAL CHANGES TO THE CLINICAL SYNDROME.
IV.—A NOTE ON CALCIFICATION IN ENCEPHALITIS LETHARGICA.

I.

EXTREMELY few autopsy findings on cases of post-encephalitic paralysis agitans have been reported.

Marinesco [11] records the case of a man, aged 43, who had an acute attack of epidemic encephalitis in March, 1920, followed by paralysis agitans; he died in February, 1922. Although lesions were found in the globus pallidus they were much more intense in the locus niger. Here the cells for the most part had undergone cytolysis and their place was shown by masses of pigment. The neuroglial cells were increased in size and number in this region, and many of them contained pigment. The nerve fibres in the locus niger had largely disappeared. The vessels showed perivascular infiltration with small round cells; and the endothelium of the capillaries contained black pigment. The region of the red nucleus appeared practically normal.

McKinley [12] reports fully the histological findings in a man, aged 51, who died of paralysis agitans of two years' duration, following an acute attack of encephalitis lethargica. The globus pallidus, putamen and caudate nucleus showed insignificant changes as compared with those found in the substantia nigra: they consisted of a moderate amount of chromatolysis and an occasional example of cytolysis, but there was no reduction in the number of cells. Slight perivascular infiltration was present in the globus pallidus but none in the putamen. In the thalamus the changes were rather more marked, but there was no evident reduction in the number of the thalamic neurones, nor was there any evidence of degeneration of nerve fibres in the basal ganglia. The lesions were most pronounced in the mesencephalon, especially in the substantia nigra; the cells were reduced to a small fraction of their normal number, and those remaining had without exception undergone chromatolysis. The pigment in the cells seemed to be increased, but this was attributed to shrinkage of the cells, which were smaller than those in a normal brain. The axis-cylinders were greatly decreased in number. A considerable amount of free pigment was scattered about and could be traced as far as the perivascular spaces. There was an increase of glia cells, and perivascular infiltration with round cells. Sections of the pons and medulla showed minimal changes.

Foix [5] reports a case in which the lesions were greatest in the substantia nigra, and consisted in atrophy of the cells with disintegration of the pigment, a process which proceeded in islets and finally resulted in cicatrization. In cases of idiopathic paralysis agitans which he has examined, the changes were most evident in the locus niger and globus pallidus, slightly predominating in the former.

Français and Lhermitte [6] report the autopsy findings in a male, aged 57, who had an attack of encephalitis lethargica in January, 1921; paralysis agitans followed in March, 1921. The patient committed suicide in September of the same year. Macroscopically depigmentation of the locus niger was noted. Microscopically the cells of the locus niger were much reduced in number and the remaining cells were distorted and depigmented. In certain parts there was no trace either of cells or of myelinated fibres. There was marked neuroglial overgrowth. The vessels of the locus niger showed perivascular infiltration with lymphocytes and plasma cells. The large motor cells of the corpus striatum were reduced in number and the remainder showed chromatolytic changes. There was considerable neuroglial overgrowth and perivascular infiltration. The small motor cells in the putamen and caudate nucleus were less affected. Lhermitte, in accordance with his pathological findings in cases of idiopathic paralysis agitans, concludes that the symptoms in this case were due to lesions in the pallidal system.

Mlle. G. Lévy [9] described the pathological changes in four cases of paralysis agitans following encephalitis lethargica. She lays stress on perivascular disintegration in the basil ganglia, producing changes resembling *l'état criblé* and *precriblé* of Vogt. Precisely similar conditions to those depicted in her book were seen in my two cases and also in the normal brain which was used as a control, and they seem to be of the nature of artefacts. Degeneration of fibres in the ansa lenticularis and in the internal capsule, and changes in the corpus Luysii, red nucleus and fields of Forel were also present. The locus niger in every case showed depigmentation. The lesions in the mid-brain were subacute. There was degeneration in the antero-lateral columns of the cord. She concludes from the widespread nature of the process in her cases that no conclusions can be drawn as to the pathogeny of paralysis agitans.

Goldstein [8] describes a case in which the changes in the substantia nigra were the most prominent feature; his article is illustrated with excellent photomicrographs.

Trétiakoff and Bremer [14] report a case of a female, aged 47, who had an acute attack of encephalitis lethargica, of the ocular type, in December, 1919; this was rapidly followed by the Parkinsonian syndrome. A relapse occurred at the end of April, 1920, with fever, generalized pains, and incontinence of urine. She died on May 29, 1920, with hyperthermia. The inflammatory lesion consisted of an increase of lymphocytes, congestion of vessels and moderate neuroglial overgrowth. These changes were most marked in the mesencephalon, and particularly in the locus niger where the number of cells was considerably reduced. The remaining cells showed various degenerative changes. The cells of the red nucleus were normal. The authors were struck by the almost complete absence of inflammatory changes in the globus pallidus; they mention, however, the occurrence of calcification in certain of the large vessels in the globus pallidus. The putamen, caudate nucleus, and cerebellum were normal.

D'Antona and Vegni [2] describe the case of a male, aged 54, who had an acute attack of encephalitis lethargica in January, 1920, followed by the Parkinsonian syndrome. He died in February, 1921. The main incidence of the disease was found to have fallen on the substantia nigra, the cells being reduced to about a tenth of their normal number; inflammatory changes, though less marked, were also found elsewhere, as in the globus pallidus and nucleus dentatus. An excellent photomicrograph depicts the changes in the substantia nigra.

Vegni [16] reports a second case in a man, aged 20, who had an attack of encephalitis lethargica, of the ocular type, in January, 1920, followed by paralysis agitans. He died in October, 1921, as a result of general peritonitis following an appendix abscess. The chief finding consisted in a great reduction in the number of cells of the substantia nigra with perivascular lymphocytosis. Degenerative changes were also found in the cells of the globus pallidus, dentate nucleus and locus cœruleus. He emphasizes the persistence of the infective process.

Gamna and Omodei-Zorni [7] report two cases. The first was that of a male, aged 29, who had an acute attack of encephalitis lethargica of the choreiform type, which was followed by the Parkinsonian syndrome. Histological examination showed an almost complete atrophy of the nerve cells of the substantia nigra and hypothalamus, associated with intense proliferation of neuroglial cells. Similar lesions, though slighter, were present in the globus pallidus, putamen, and caudate nucleus.

The second case was that of a woman, aged 27, in which the Parkinsonian syndrome did not become apparent for nearly two years after an acute attack of encephalitis lethargica. Lesions similar to those in the first case were found in the substantia nigra; the subthalamic region was very slightly altered and the corpus striatum was unaffected.

Urechia [15] reports the case of a male, aged 44, who for a year suffered from insomnia and periods of psychomotor excitement. There were no definite signs of organic disease in the central nervous system, except that his pupils were unequal and fixed. Although the Wassermann reaction was negative, he was given anti-specific treatment in view of the pupillary condition. Seven months later he presented definite signs of the Parkinsonian syndrome and a retrospective diagnosis of encephalitis lethargica was made. The patient died shortly afterwards. An autopsy showed intense inflammatory lesions in the basal ganglia, especially in the globus pallidus, corpus Luysii, and substantia nigra; less marked lesions were also present in the dentate nucleus.

II.

Histological Findings in Two Cases.

The following are the only two cases as yet in which I have had the opportunity of pathological study:—

Case 1.—A male, aged 41, came under observation in September, 1922, with well-marked paralysis agitans.

His wife stated that he had been quite well until an acute illness in May, 1921, characterized by double vision and marked sleeplessness. For more than a week he slept day and night and had great difficulty in swallowing. He was acutely ill for four weeks; it was then noticed that he was stiff and had considerable difficulty in moving. He improved, but was troubled with drowsiness for some months. The rigidity gradually became worse, so that feeding or dressing himself was impossible.

Examination in September, 1922, showed a very marked condition of paralysis agitans. It was impossible to understand his speech owing to the feeble voice; he was unable to dress and feed himself, and could scarcely move in bed; his head was slightly retroflexed, his mouth open, and he had marked sialorrhœa. His eyes had a staring expression. The pupils were regular in outline, equal and centrally placed; both reacted well to light and accommodation. The ocular movements were full and were carried out nearly as promptly as by a normal person, but there were a few initial nystagmoid movements in the extreme lateral positions; convergence was normal. The fundi were normal. Voluntary movements of the facial and jaw muscles were carried out feebly and slowly. There was slight weakness of the lower face on the right side which was apparent only on voluntary movement, as in showing the teeth. The tongue was protruded with difficulty, and was flabby and tremulous. The palate moved somewhat feebly on phonation. There was considerable difficulty in swallowing. The muscles of the neck were hypertonic, and there was loss of associated head and eye movements.

The posture of the arms was typical of paralysis agitans, especially that of the hands. The tone was considerably increased in all muscle groups, and the "cogwheel" phenomenon was well marked. All movements were carried out slowly and with difficulty. The reflexes were brisk and equal on the two sides.

At times there was a very slow rhythmical tremor of the true paralysis agitans type in both hands, the chief movement being one of alternating flexion and extension of the fingers. The rate of the tremor was four to the second. It was observed only when the limbs were at rest and never during voluntary movement. The musculature of the abdomen was hypertonic, the abdominal reflexes being excessively brisk. The posture of the legs was one of extension at the knees with the toes pointed downwards and the feet inverted; as in the arms there was moderate loss of power and tone was markedly increased in all muscle groups, but predominated in the post-tibial group of muscles and in the extensors of the knee.

The deep reflexes were brisk and equal; there was no ankle clonus; the right plantar reflex gave a doubtful extensor response, while the left was normal in type.

There was no disturbance of sensation in the arms, trunk or legs.

Progress.—The patient improved under hyoscine; his speech became clearer and he was able to turn more easily in bed.

On September 26 there was a rise in temperature with an accompanying increase in the respiration and pulse rate. The pyrexia became progressively greater and on the day of his death—the 29th—the temperature was 104·6° F., respiration 60, and pulse 150. There was no clinical evidence of pulmonary implication.

An autopsy was performed ten hours after death. No abnormality was noted in the meninges. The brain and spinal cord were hardened in 10 per cent. formalin-saline for fourteen days.

A series of six horizontal sections was made through the basal ganglia, the thickness of each slab being approximately 4 mm. A portion of the tissue, including the basal ganglia, was taken from each slab and numbered; those from one-half of the brain being treated by the Weigert-Pal method, and those from the other by alum hæmatoxylin and van Gieson, and by Nissl's method. Photographs of each slab were taken for reference.

The mid-brain was cut in serial sections.

The brain from a man aged 40, who died as the result of an accident, was used as a control and was treated in precisely the same manner as the brain under consideration, the levels of the horizontal sections being approximately identical.

Histological Findings.

Cerebral cortex.—Beyond capillary dilatation there was no appreciable deviation from the normal. The cells were normal except for very occasional cytolysis. There was no diminution in the number of cells, nor was any perivascular infiltration observed.

Basal ganglia.—It may be said at the outset that no marked pathological changes were found in this region. The cells in the caudate nucleus and putamen were for the most part normal and were not appreciably diminished in number. Cytolysis was occasionally seen, especially in the putamen. Many of the cells stained poorly, were ballooned and had eccentric nuclei. Capillary dilatation was general. For the most part the vessel walls were normal, except for an occasional increase of cellular elements in them. Perivascular infiltration with round cells was not pronounced, but each section showed a few examples of this. There was no appreciable glial cell overgrowth.

Globus pallidus.—Many cells stained palely; chromatin granules were not apparent in the majority of the cells. This absence of chromophilic staining was noticed in all the cells of the basal ganglia and also in the control brain, and probably depended on faulty fixation. The vast majority of the cells were in every respect normal; rarely a cell with a markedly eccentric nucleus and an indefinite outline could be seen.

There was no diminution in the number of the large polygonal cells. The cells in ten consecutive fields were counted, and this was also done in sections from the corresponding blocks of the normal brain. Two different levels were taken, one from the middle of the lenticular nucleus and the other towards its caudal extremity. In each case the count from Case 1 exceeded that of the normal control.

The majority of the cells in the globus pallidus, and incidentally those of the thalamus, showed a collection of pigmented granules which usually occupied half the cell. They stained green with toluidin blue. They were also present in the cells of the control though not to the same extent, and stained yellowish instead of green. In sections stained by Scharlach red they appeared as reddish granules in the cells, which points to the possibility of their being of the nature of lipochromes. Granules also could be seen scattered about in the surrounding tissue, and could be traced to perivascular lymphatic spaces. Similar appearances, though less marked, were also seen in the normal brain.

The vessels of the globus pallidus shared in the general vascular dilatation; occasionally perivascular infiltration by lymphocytes was observed, but this was only slightly more common than in the putamen and caudate nucleus. The walls in many instances showed an increase in the cellular elements.

In the sections stained by alum hæmatoxylin and van Gieson's counterstain, well-marked calcareous degeneration was observed in the walls of certain vessels. Such vessels were few in number, and were only seen in sections from about the middle of the basal ganglia. Further, the affected vessels were situated in the anterior portion of the globus pallidus and were evidently ascending vessels from the anterior perforated spot. In this region the arteries, veins and capillaries were all affected. In the majority of the vessels the deposit lay between the adventitia and the media. Hyaline degeneration was evident in the walls of those vessels that were only slightly affected; in some of these the deposit could be seen in the Virchow-Robin space. There was no thrombosis in any of the affected vessels. In the smaller vessels the cellular elements in the vessel walls were increased.

Thalamus.—The cells were not diminished in number. Cytolysis was relatively common, but the cells were for the most part otherwise healthy. Pigmentation granules were present in the majority of the cells. Perivascular infiltration was seen about as frequently as in the globus pallidus.

Sections from the lower three slabs showed acute changes in the subependymal region of the thalamus, and in that portion of the subthalamic region which adjoins the third ventricle. These changes consisted of numerous recent hæmorrhages in the perivascular spaces and surrounding tissue. Perivascular infiltration was here more marked than anywhere in the basal ganglia; similar acute changes were also noted in the infundibulum.

Corpus Luysii.—The cells appeared normal.

Sections stained by the method of Weigert-Pal showed no evidence of degeneration in the systems of fibres connected with the corpus striatum.

The mid-brain.—In this region the changes were distinctly more marked than in the basal ganglia, the greatest incidence of the disease having fallen on the substantia nigra. The pigmented cells were reduced to a small fraction of their normal number, and in their place were scattered particles of pigment which varied considerably in size. The few cells that remained showed various degenerative changes, such as eccentric nuclei, extrusion of the pigment, vacuolization and loss of the normal processes (fig. 2). Macro-

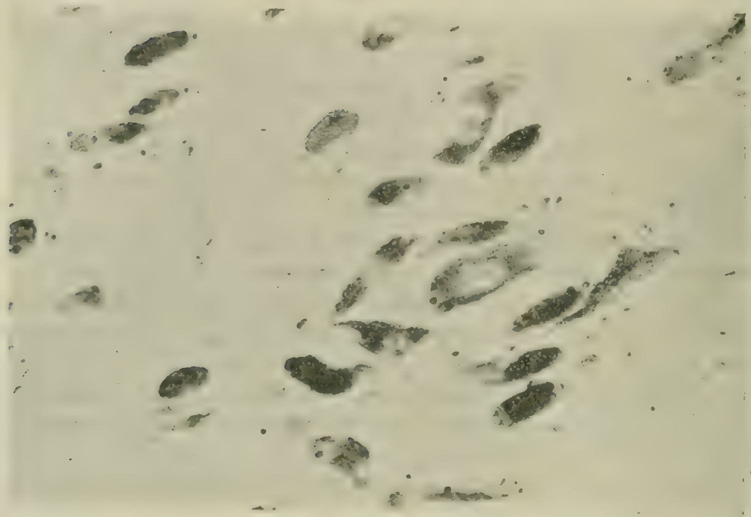

Fig. 1.—Photomicrograph × 300. Pigmented cells of normal substantia nigra.

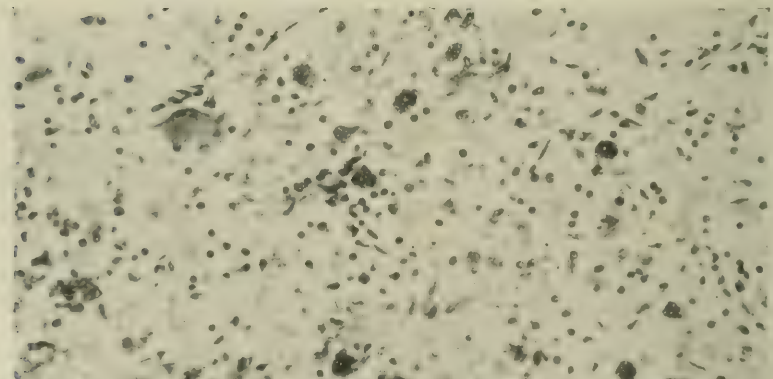

Fig. 2.—Photomicrograph × 300. *Case* 1. Parkinsonian syndrome of eighteen months duration. Substantia nigra showing marked reduction in the number of pigmented cells and scattered masses of free pigment. The two remaining cells in this field show cytolytic changes.

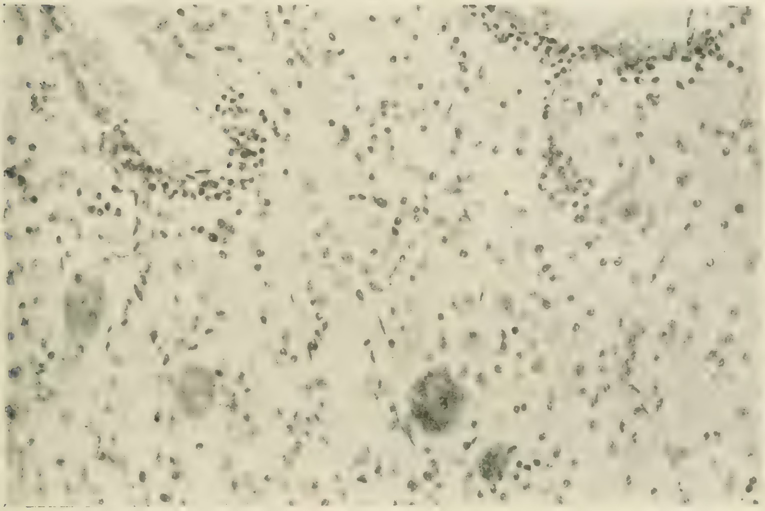

FIG. 3.—Photomicrograph × 300. *Case* 1. Perivascular lymphocytosis in region of substantia nigra, in addition to cytolytic changes in the cells.

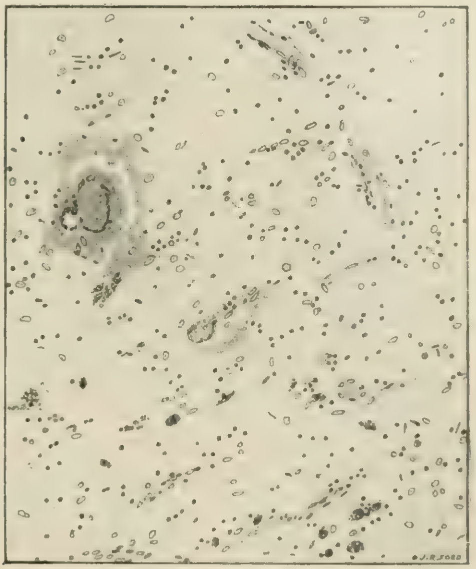

FIG. 4.—Camera lucida drawing × 100. *Case* 1. Recent perivascular hæmorrhages in region of substantia nigra.

and microphages of glial origin were plentiful, and many were packed with pigment. They could be traced to the perivascular spaces. In the walls of the larger meningeal veins in the interpeduncular space there were numerous particles of pigment; these also were evident in the lumen of the vessels, usually in the interior of the macrophages. Pigment was also present in these veins in the control brain, but it was in very much smaller amount than in this case. Perivascular infiltration was more prevalent in the mid-brain than in the basal ganglia (fig. 3). A few of the vessels showed hyaline degeneration of their walls.

Numerous recent hæmorrhages, similar to those described above as occurring in the thalamus, were present, especially in the ventral half of the mid-brain (fig. 4).

The glial cell overgrowth was not accompanied by a parallel increase in the glial fibres.

The cells of the *locus cœruleus* were not diminished in number; a few were depigmented and a small proportion of them showed chromolytic changes. The cells of the *third nucleus* appeared normal.

The smaller cells of the *red nucleus* were normal, except for fairly well-marked cytolysis. Some cells of the pars magno-cellularis showed definite changes, such as vacuolization, and several contained greenish granules of pigment; only a few of these cells appeared healthy. There was no apparent reduction, however, in their number.

Sections from the *pons* and *medulla* showed capillary dilatation and very moderate perivascular infiltration. No hæmorrhages were apparent. The cells of the nuclei of the lower cranial nerves were for the most part healthy, although in some there were chromolytic changes.

Sections from the cervical and dorsal regions of the cord were normal.

The Weigert-Pal method in sections from the pons and medulla showed no evidence of tract degeneration.

Case 2.—Female, aged 68, came under observation in February, 1923, with a condition of well-developed paralysis agitans.

She stated that she had been in good health until an attack of "influenza," about January, 1920. This illness was characterized by headache, pains all over, and marked sleeplessness. She also noticed that when she looked at anything close, as in reading, the letters ran together; she had never previously been troubled in this way. She gradually improved and at the end of a month was able to get up, but "she had never felt the same since." A few months later she noticed that she could not move her arms so quickly as formerly, and that she had a difficulty in getting upstairs. Somewhat later a tremor appeared in the left hand. In January, 1921, she suddenly lost the use of both legs. She remained in bed one month and the power of the legs gradually returned. In February, 1922, a similar attack occurred, from which she recovered fairly well.

On examination she showed a condition of moderate general rigidity with Parkinsonian facies. Her speech was slow and monotonous. The pupils were unequal, the left being larger than the right; there was a definite right ptosis; this condition in the right eye was considered to be due to paresis of the right cervical sympathetic. The pupils reacted moderately well to light; but there was no reaction on accommodation. Convergence was much limited, otherwise the ocular movements were full.

The jaw and facial movements were feeble and slowly performed. There was slight weakness of the lower face on the left side.

The limbs on both sides showed the characteristic rigidity of paralysis agitans, but this was much more evident in the limbs on the left side. Power was considerably diminished and movements were performed slowly. There was tremor in both arms, rapid, coarse and exaggerated by movement.

The reflexes were more active on the left side, and ankle-clonus could be obtained on this side. The left plantar response was indefinite, whilst the right was probably flexor.

Examination of the heart showed evidence of left-sided enlargement; this was attributed to the general arteriosclerosis which was present. (Blood-pressure: systolic 240, diastolic 140 mm. Hg.)

A diagnosis of paralysis agitans, probably post-encephalitic, was made.

Course.—The patient improved on hyoscine, but on February 16 suddenly became acutely ill with dyspnœa and pyrexia; the temperature progressively rose and reached 104° F. on the third day when death occurred. Despite tachypnœa, no adequate signs to account for the symptoms could be found in the lungs. The cardiac condition showed no appreciable alteration from that present when she first came under observation.

An autopsy was performed six hours after death. Only the brain was removed. The membranes showed no gross abnormality.

The brain was hardened for ten days in formalin-saline and was then treated in a precisely similar manner to the brain of Case 1.

The following were the principal histological findings. All the cerebral arteries showed advanced arteriosclerosis.

Cerebral cortex.—Normal, no calcification of vessels.

Cerebellum.—Cells of Purkinje appeared healthy and the dentate nucleus was normal. No calcification or inflammatory changes were present.

Caudate nucleus.—Vessels shared in the general arteriosclerosis, the lumen of one or two of the arterioles was completely obliterated. Several of the vessels showed perivascular infiltration with round cells and capillary dilatation was general. The cells seemed normal except for pigment granules and occasional satellitosis.

Putamen.—A comparatively large hæmorrhage, not of recent origin, was seen in the anterior part of the putamen at its junction with the globus pallidus; the hæmorrhage partially involved the latter in its anterior part. Except in these areas the cells seemed normal. The vessels showed changes similar to those in the caudate nucleus.

Globus pallidus.—The anterior portion was partially involved in the hæmorrhage mentioned above. Some of the vessels showed well-marked perivascular infiltration with round cells, but none of them were thrombosed. A few vessels in anterior half of the globus pallidus showed calcification of their walls. Except for the small area involved in the hæmorrhage the rest of the globus pallidus contained healthy motor cells, except for pigmentation and occasional satellitosis.

Internal capsule (right).—The anterior part of the posterior limb was slightly involved in an old hæmorrhage of moderate size which affected the thalamus mainly.

Thalamus.—The old hæmorrhage occupied the outer part of the thalamus and was of moderate size; another small area showed an almost complete absence of thalamic cells. The remainder of the cells of the thalamus appeared healthy except for pigmentation. A number of quite recent perivascular hæmorrhages were present on the inner wall of the thalamus adjoining the third ventricle.

Subthalamic region.—Perivascular hæmorrhages were prominent, especially around the third ventricle. A few of the vessels showed definite perivascular infiltration with small round cells. (An accident occurred to the Weigert-Pal blocks from the basal ganglia on the left side and also to the block from the subthalamic region, so that no Weigert-Pal sections were obtained from these regions.)

Mid-brain.—The substantia nigra showed no perceptible reduction in the number of cells on either side, though a slight degree of depigmentation had taken place. A few of the vessels showed inflammatory changes, but there was no evidence of glial cell proliferation.

Pons, *medulla* and *cervical* region of the cord showed no changes of note. Weigert-Pal sections of these regions showed, however, a slight but definite lesion of both pyramidal tracts.

Summary of Histological Findings in the Two Cases.

(1) In both cases subacute inflammatory changes were found; in Case 1 these were more prominent than in Case 2, and were most marked in the mesencephalon. In Case 2 the changes were slighter and were more evident in the basal ganglia and subthalamic region than in the mid-brain.

(2) In Case 1 there was a marked diminution of the cells of the substantia nigra on either side; in Case 2 the cells showed no reduction in number.

(3) The mode of death in both cases was strikingly similar, namely a sudden onset of pyrexia and tachypnœa *which were progressive.* Mlle. G. Lévy, in her recent book on the late manifestations of encephalitis lethargica, also describes this mode of death in four cases of advanced Parkinsonism. In neither of the two cases above described were

changes found in the medulla to account for the marked increase in the respiratory rate, and no signs were observed in the chest in either case during life sufficient to account for the tachypnœa. The perivascular hæmorrhages were similar in both cases and occurred in practically the same locality, i.e., around the third ventricle. It seems probable that these acute changes indicated a sudden flaring up of the morbid process, and that this was the immediate cause of death.

In both cases calcareous deposits were observed in the walls of the vessels in the anterior part of the globus pallidus and in this region only.

III.

Pathogenesis of Paralysis Agitans.

No attempt will be made here to discuss fully the pathogenesis of paralysis agitans. There are at present two opposing schools of thought. The one represented by the Vogts, Lhermitte, Ramsay Hunt and others, consider that the causative lesion in idiopathic paralysis agitans lies in the globus pallidus.

The other, led by Trétiakoff [13], who is supported by Pierre Marie, thinks that the symptomatology of this condition is dependent on disease of the substantia nigra. Trétiakoff bases his opinion on a close study of the substantia nigra in twenty-nine cases representing a variety of organic diseases, inflammatory and otherwise, of the central nervous system. In twenty of these cases he found no changes in this region. In all the cases of idiopathic paralysis agitans which he examined, numbering nine, he found degenerative changes in the substantia nigra; he further states that in the type of acute encephalitis lethargica characterized by katatonia he has found similar changes in this region. He also describes a case in which a unilateral lesion of the locus niger was accompanied by paralysis agitans affecting the limbs on the opposite side only.

Lhermitte and Cornil [10], on the other hand, in seven cases of disease other than paralysis agitans, i.e., combined sclerosis of specific origin, syringomyelia, cerebral tumour, two cases of complete section of the cervical region of the cord and senile dementia, state that they found alteration in the cells in the substantia nigra in all the cases. Trétiakoff, in reply to these criticisms, emphasizes the importance of three concomitant factors in such cases: (1) the physiological state of the patient; (2) the condition of the other systems of fibres, especially the pyramidal system; (3) the time elapsing between the occurrence of the lesion and the death of the patient.

I have examined the substantia nigra in one case of each of the following diseases: myasthenia gravis, cerebral syphilis, subacute combined degeneration of the cord, primary dementia, myotonia atrophica, and recurrent cerebral hæmorrhage. In none of these cases did I find a diminution of the number of the cells, or depigmentation of pathological importance.

Three cases of idiopathic paralysis agitans were also examined from this point of view, and in all three cases a normal substantia nigra was found on both sides.

The substantia nigra in three cases of encephalitis lethargica, fatal in the acute stage, was found to be markedly affected; the reduction in the number of cells and the scattered masses of pigment being striking (fig. 6).

In Case 1, as previously described, the degenerative changes in the locus niger were very marked, and contrasted well with the relative paucity of the lesions in the globus pallidus.

In Case 2 the substantia nigra showed nothing abnormal beyond very slight depigmentation, and it is certain that the marked condition of rigidity which was present did not depend on a lesion in this region. I do not wish to emphasize this case as one of encephalitis lethargica in which the substantia nigra was normal. I am not certain that the paralysis agitans in this case depended on the attack of encephalitis lethargica, because large hæmorrhages, which were obviously due to primary arterial disease, were present in the basal ganglia on the right side and involved the globus pallidus.

In more than half the cases of the Parkinsonian syndrome following encephalitis lethargica which have come to autopsy, changes in the substantia nigra were definitely stated to be the most prominent pathological finding; moreover, in every case some degenerative change affecting the cells of the substantia nigra was found. Case 1 showed these changes in a marked degree.

We may surmise then that in idiopathic paralysis agitans a lesion of the globus pallidus, or possibly of the subthalamic structures with which it is connected, is the usual pathological basis of the disease; whereas post-encephalitic Parkinsonism is usually due to degeneration of the substantia nigra.

IV.

CALCIFICATION IN ENCEPHALITIS LETHARGICA.

Buzzard and Greenfield [1] in 1918 were the first to note the occurrence of calcification in encephalitis lethargica. The case was that of a young woman of 28 who died six months after an acute attack of this disease. Calcification of a few vessels in the cortex, and more particularly of the vessels of the globus pallidus, was described by them.

Dürch [3] in 1921 found calcification in twelve out of fifteen fatal cases of encephalitis lethargica. The ages of the patients ranged from 30 to 60 years. Death occurred in one case as early as the eighth day.

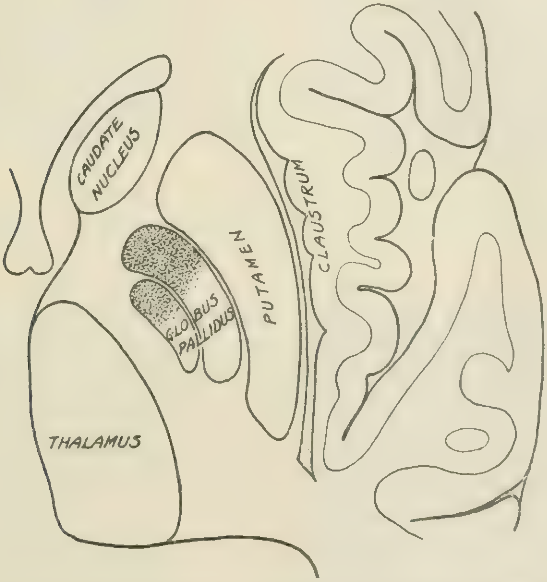

FIG. 5.—Diagram of basal ganglia. Dotted area indicates the region principally affected by calcification in encephalitis lethargica.

He described three forms of calcification: (1) calcification of vessels; (2) globules of calcium lying free in the supporting tissue; (3) calcification of nerve cells, this being the rarest form.

The calcification of vessels occurred most frequently in the corpus striatum, but also was found in the nucleus dentatus, hippocampus, cornu Ammonis, hemispheres and optic thalamus.

The calcified globules were most commonly observed in the hemispheres, less often in the corpus striatum, and occasionally in the corpus callosum, gyrus hippocampi, optic thalamus and medulla oblongata.

I have examined the brains of six fatal cases of encephalitis lethargica, three dying in the acute stage and three a year or more after the original attack. In all six cases calcification in varying forms was found.

In all the cases, except one, the process was limited to the anterior part of the globus pallidus (fig. 5).

Case 1.—A case of paralysis agitans, has already been described fully. As previously mentioned the basal ganglia were cut horizontally into six slabs and numbered accordingly, No. 1 being uppermost, i.e., through the head of the caudate nucleus.

In sections from slab 4, i.e., through the middle of the globus pallidus, well marked calcification was found in the majority of the vessels in the anterior half of the globus pallidus. The vessels in this region in sections from slabs 3 and 5 showed hyaline degeneration, chiefly of the media, but no deposit of calcium salts in their walls. The cortex from several regions of the cerebellum and hemispheres was carefully examined, but no similar changes in the vessel walls were observed.

In addition to the change in the vessels, a number of mulberry shaped globules, staining dark brown with hæmatoxylin, were noted (Plate, figs. 1 and 3).

Case 2.—A case of paralysis agitans showed moderate calcification of vessels in the anterior half of the globus pallidus. This change was not present in sections from slab 6, i.e., the lowest part of the globus pallidus. No mulberry-shaped or calcified globules were observed, nor any fatty globules in frozen sections of the globus pallidus stained by Scharlach R.

Case 3.—Male, aged 20, was admitted to the National Hospital on December 29, 1922, under the care of Dr. J. Collier, to whom I am indebted for permission to publish the case.

According to his father the patient seemed in his ordinary good health until December 26, 1922, when he complained of feeling "out of sorts." He remained at home on the 27th and 28th, but he did not go to bed or complain of any further symptoms. On the morning of the 29th he was found by his father unconscious in bed and later he had a fit.

On admission to the National Hospital he was unconscious, but responded by movements of the limbs to painful stimuli. Breathing was stertorous. Salivation excessive. Temperature 102° F. Pulse 100. Respirations 30. The pupils were noted as small and reacted poorly to light. The right side of the face moved less well than the left. There was no paresis of the limbs. The arms were flexed and held rigidly across the chest. The deep reflexes were active; the abdominal reflexes were absent; the plantar response on each side was extensor in type.

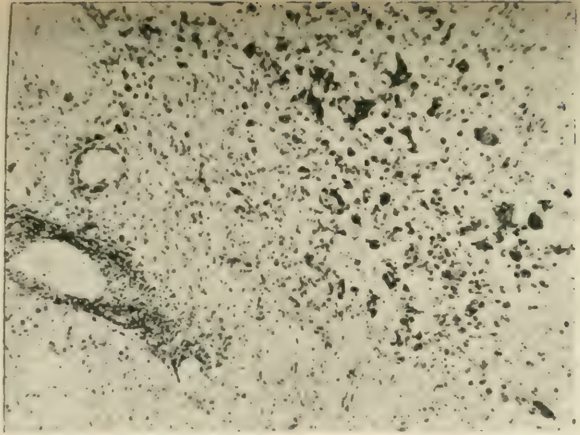

FIG. 6.—Photomicrograph × 100. Acute encephalitis lethargica. Section from mid-brain showing marked reduction in number of pigmented cells of substantia nigra and scattered masses of pigment.

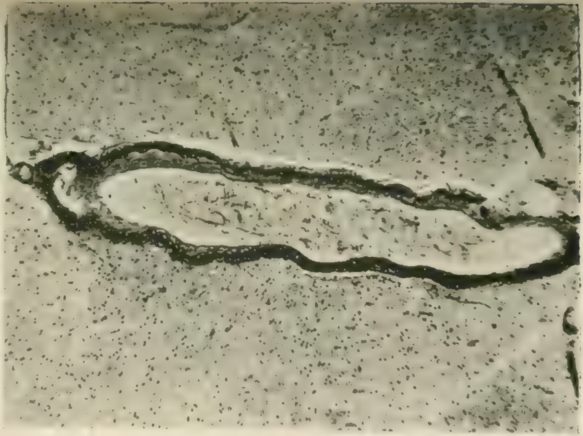

FIG. 7.—Photomicrograph × 80. *Case* 3. Acute case of encephalitis lethargica in a young man aged 20, death occurring on the fourth day. Calcification of a vessel in anterior part of globus pallidus.

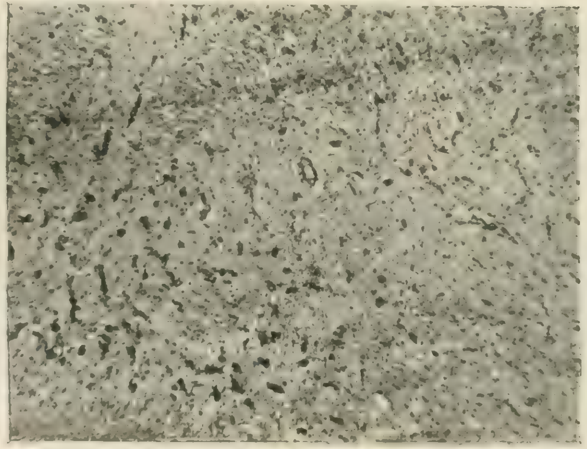

FIG. 8.—Photomicrograph × 80. *Case* 4. Acute encephalitis lethargica. Section from basal ganglia, stained with hæmatoxylin and van Gieson, showing calcified globules in globus pallidus.

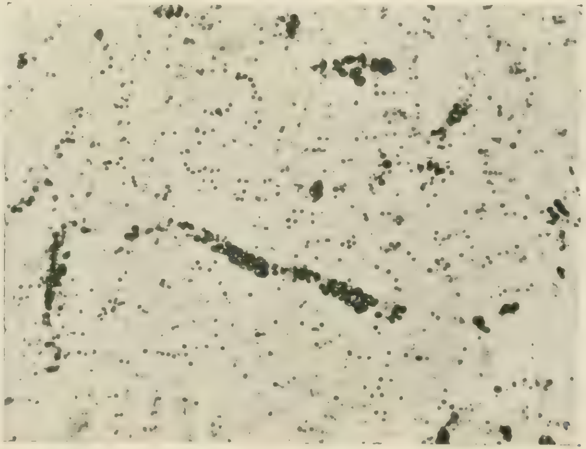

FIG. 9.—Photomicrograph × 160. *Case* 5. Chronic case of encephalitis lethargica. Calcified globules in globus pallidus.

At 8 p.m. on the 29th he had a generalized convulsion and another at 1 a.m. on the 30th. He died during the course of that day.

An autopsy showed typical findings of an acute encephalitic lethargica, namely, general vascular dilatation, perivascular hæmorrhages, and moderate round-celled infiltration. These changes were much more marked in the basal ganglia and cortex generally than elsewhere. The mid-brain showed very few changes, and the substantia nigra was normal.

In addition to these findings certain changes were present in the anterior half of the globus pallidus, namely: (1) hyaline degeneration of the vessels mainly affecting the media; (2) early calcification in a number of the arteries and arterioles (fig. 7 and Plate, fig. 5); (3) mulberry globules, similar to those mentioned in Case 1 (Plate, figs. 1 and 3). Sections from the cerebellum and cerebral cortex showed no similar affection of the vessels.

Case 4 was a case of encephalitis lethargica in which death occurred in the acute stage. Unfortunately all details of the illness are missing and cannot be traced.

The histological findings were as follows: Well marked inflammatory changes typical of acute encephalitis lethargica, i.e., general vascular infiltration with round cells and typical "cuffing." These changes were present in cortex, cerebellum, basal ganglia, brain-stem and cord, but were most marked in the mid-brain. There was considerable destruction of the cells of the substantia nigra. In addition to these findings there was present calcification of vessels in the anterior part of the globus pallidus and to a less extent in the cerebellum.

In the globus pallidus were seen calcified granules of small size, lying free in the supporting tissues and ranged along the capillary walls (fig. 8). In frozen sections from the basal ganglia on the opposite side, stained with Scharlach R., the earliest stage of these globules could be seen in the form of fatty globules. These were confined to the anterior half of the globus pallidus. (Plate, figs. 1 and 2.)

Case 5.—The histological investigation of this case was carried out by Dr. J. P. Martin, to whom I am much indebted for permission to examine his sections.

Female, aged 25, was admitted to the National Hospital in April, 1921. In April, 1920, she had an attack of encephalitis lethargica. She improved slowly, but in August of the same year she commenced to have repeated tonic contractions of certain muscles of the trunk, and these persisted.

On examination she showed a somewhat expressionless face with a flexed posture of the arms, suggesting an early Parkinsonian syndrome. The respiratory rate was constantly increased and averaged 40 to the minute.

In addition she had constant involuntary movements of both shoulders, the left being more affected than the right. The movements were due to spasmodic contraction of the latissimus dorsi. During the last six weeks of the illness there was continued pyrexia. Death took place on June 18, 1921.

The principal histological findings were as follows: (1) The mid-brain showed no changes of note beyond slight depigmentation of the substantia nigra and a slight reduction in the number of cells. (2) The subthalamic region showed a number of recent perivascular hæmorrhages in the region of the third ventricle; these were similar in all respects to those found in cases 1 and 2. (3) The basal ganglia presented no marked lesions except gross calcifications of the vessels and many calcified globules in anterior half of the globus pallidus (fig. 9 and Plate, figs. 1, 4 and 6). The cortex and cerebellum showed minimal changes, but no evidence of calcification was found elsewhere than in the globus pallidus.

Case 6 was a child, aged 7, who died on the tenth day of an acute attack of chorea, which may have been a manifestation of encephalitis lethargica. In the brain, in addition to mild inflammatory changes, there was definite calcification of a few medium-sized arteries in the anterior part of the globus pallidus, and mulberry globules in the putamen and globus pallidus. The vessels of the cortex of the hemispheres and cerebellum showed no calcification.

As controls for the occurrence of calcification in the globus pallidus brains of persons dead with the following conditions were examined: An accident, cerebral tumour (two cases), sub-acute combined degeneration of the cord, transverse lesion of the cord in the cervical region, Huntington's chorea, and three cases of idiopathic paralysis agitans.

In the case of Huntington's chorea well-marked calcification of vessels was found in the anterior part of the globus pallidus, but in no other situation; mulberry globules were also observed in the basal ganglia.

In all three cases of idiopathic paralysis agitans there was calcification of the vessels in anterior part of the globus pallidus. In none of the other cases examined were such changes seen.

The Vogts in their latest monograph on diseases due to pathological changes in the basal ganglia make mention of only one case showing calcification of vessels and of globules such as were present in the cases described above. This was a case of Westphal's, who died in 1918 after a seven weeks' illness characterized by athetotic movements, and later by dysarthria, dysphagia, retropulsion and general rigidity. The history and photomicrographs strongly suggest an attack of encephalitis lethargica, although no mention is made of this diagnosis in the text.

From the findings in the six cases described above it is evident that calcification occurs almost constantly in the globus pallidus in acute and chronic cases of encephalitis lethargica. In all six cases calcification of the vessels was observed, and in five out of the six cases globules, either fatty, or in mulberry form, or fully calcified, were seen. Further, it must be emphasized that these changes were localized in every case except one (No. 4) to the anterior half of the globus pallidus, which area is supplied by internal striate branches of the middle cerebral artery. These changes will now be considered more fully.

Calcification of Vessels.

This may appear at a very early stage of encephalitis lethargica, i.e., on the fourth day of the illness in Case 4. Dürch [3] found the condition present in a patient who died on the eighth day.

Age seems to play no part in its production, as Case 6 was aged seven, and two of the other cases were under the age of thirty years.

The changes in the vessel wall preceding the deposition of calcium salts may be of two kinds: (1) a hyaline degeneration chiefly of the media, which becomes swollen and loses some of its nuclei; (2) a fatty degeneration of the vessel wall, the fatty globules appearing in the Virchow-Robin space, or more rarely in the media. These processes do not as a rule occur together in the same vessel, hyaline degeneration being the commonest.

The earliest deposits of calcium usually occur between the adventitia and the media. In vessels slightly affected the deposit may be seen in only a portion of the wall. The calcium is deposited in the form of granules uniformly small in size. The media is then invaded, and the granules coalesce to form solid plaques which entirely surround the vessel. The elastic lamina, in vessels in which the process is advanced, may be broken up in places and the granules may be seen immediately under the intima, but this is rare and the intima is usually spared. In addition to the deposit between the adventitia and the media, and in the media itself, vessels are sometimes seen surrounded by a number of small calcified granules which have invaded the Virchow-Robin space.

The lumen of the vessel is as a rule unaltered. One vessel in Case 5 was seen to be thrombosed, and the thrombus consisted entirely of calcium salts. Arteries and capillaries of all sizes may be affected; the veins less constantly show this change. There is rarely a concomitant perivascular infiltration of the vessels with round cells.

Fat globules.—In only one case (Case 4) was an opportunity afforded to study the earliest stages in the formation of these calcified globules. This was a case in which death occurred during the acute stages of the disease.

In frozen sections of the basal ganglia stained with Scharlach R., a large number of fatty globules were seen in the anterior half of the globus pallidus. No other parts of the basal ganglia were thus affected. These globules varied considerably in size from 1-2 μ up to 20 μ or more. They lay free in the supporting tissue; many were aggregated along the walls of the capillaries. About half the number of globules seen were solid; the remainder showed varying degrees of vacuolation. The majority had a darker staining periphery (alum hæmatoxylin was used as a counterstain) and some in addition showed a second darkly staining ring in the substance of the globule, which gave it the appearance of possessing a nucleus. Most of the globules were round in form and were regular in outline. Some showed a crenated edge, and in them more darkly staining portions were usually seen. In a few the fatty element staining with Scharlach R. was replaced almost entirely by a blue-black mass which stained with hæmatoxylin, and which presumably consisted of calcium salts. All intermediate stages in pigmentation of the fatty globules were observed (see Plate, figs. 1 and 2).

In celloidin sections from the basal ganglia of the opposite side in this case, fully formed calcified globules were seen in the globus pallidus (fig. 8).

An attempt was made to determine the nature of the fat composing the globules.

Methods.—(1) Frozen sections were stained with Scharlach R., osmic acid, and Nile-blue sulphate.

(2) Frozen sections submitted to the action of fat solvents, e.g., acetone, ether, xylol, were treated as above.

(3) Bell's modification of the Dietrich-Ciaccio method.

(4) Hæmatoxylin after mordanting with bichromate.

(5) Bichromate-osmic acid method.

(6) Behaviour in polarized light.

With Scharlach the globules stained well, but as previously described, varying degrees of pigmentation, commencing at the periphery of the globule, were seen.

The globules remained unaltered after treatment with fat solvents; an attempt was made to remove the pigmented outer ring of the globules by a 3 per cent. solution of acetic acid, but sections so treated showed the same resistance to the fat solvents mentioned.

The globules stained moderately well with osmic acid, the periphery of the globule always stained the most deeply. With the bichromate-osmic acid method, the same results were obtained.

With Nile-blue sulphate the globules stained pink, but this may have depended on the long formalin fixation.

Sections stained by Bell's method showed similar results to those stained simply by Scharlach R.

The globules in unstained and stained sections showed no double refraction with polarized light.

Conclusions.

It is evident from these results, many of which are contradictory, i.e., the behaviour of the globules in presence of fat solvents and polarized light, that we are here dealing with fat substances which differ in several ways from those occurring in morbid conditions in other parts of the body.

The globules seem to remain unaltered throughout the various tests. What is there in these globules which differs from other fatty deposits elsewhere? It would seem that the answer to this question lies in the presence of the pigmented envelope which surrounds the globules; this was sometimes observed as a mere ring, but many globules showed an extension of this process inwards (Plate, fig. 1). This protective covering probably prevents the contained fatty substance in the globule behaving as an ordinary fat when subjected to the usual tests.

Emrys-Roberts and Haig [4] have described in a recent paper the occurrence of similar pigmentary changes in fat globules which they have observed in the myocardium, kidney and liver in fatal cases of fulminating diphtheria and subacute septicæmia. They describe the fatty granules as occurring in cells undergoing degenerative changes; these globules then may leave the damaged cells and appear in the surrounding tissue. A further stage then occurs, namely an alteration in the fatty or lipoidal globules whereby a progressive loss of fatty contents is accompanied by a gradual deposition of pigment at the periphery of the globules; a shrinkage process follows, resulting in the formation of minute deeply pigmented spheroidal granules. They investigated the nature of the fat content of these globules by a large variety of methods and stated as a result of their findings that these bodies were present unaltered morphologically and functionally in all frozen and paraffin sections both stained and unstained.

The resemblance between the bodies described by these two observers and the fatty globules in encephalitis lethargica is striking, and it seems probable that we are dealing with a similar alteration in the fatty contents of the globules and bodies, though there is no indication as far as I have observed that the fatty globules in encephalitis lethargica originate from degenerated cells.

Calcified globules.—In three of the six cases examined (1, 3, and 6), in sections stained by hæmatoxylin and van Gieson a number of globules were seen lying free in the supporting tissue in the anterior half of the globus pallidus, and in two of the cases also in other parts of the basal ganglia. These bodies stained varying shades of brown; some showed a blue-black nucleus. In shape they somewhat resembled a mulberry, and have already been referred to as mulberry globules (Plate, figs. 1 and 3). These bodies are formed by the fusion of several globules, and may be as large as 50 μ to 60 μ. Small single round globules, staining in a similar manner, may be seen lying along capillary walls. From the resemblance in size and shape to the fully calcified globules (*vide infra*), and also from the presence in some of them of a blue-black nucleus, it was thought that these mulberry bodies were possibly transitional forms between the fatty globules and the calcified globules, but it seems as likely that they may form an alternative process to the calcified globules.

The latter were found in two out of the six cases in sections stained by hæmatoxylin and van Gieson. In Case 4 the occurrence of fatty globules has already been described; in sections from the basal ganglia of the opposite side small fully calcified globules were seen lying free in the supporting tissue in a small area in the anterior half of the globus pallidus (fig. 8). In Case 5 similar globules, though more numerous, were found in the same part of the globus pallidus (fig. 9 and Plate, figs. 1 and 4). In both cases there was an accompanying calcification of the vessels. These globules stain homogeneously blue-black with hæmatoxylin; they occur singly as small globules 2μ to 15μ in diameter, or in large "knobby" masses 50 μ to 60 μ in size. The majority of the globules were seen to lie along the walls of the capillaries, and often as minute granules around the larger vessels.

THE OCCURRENCE OF CALCIFICATION IN THE BRAIN IN OTHER CONDITIONS.

In arteriosclerosis, especially the senile form, deposits of calcium salts in the media are not of uncommon occurrence. They also occur in corpora amylacea and in psammomatous tumours.

Dürch has found calcification of the cerebral vessels in the brain of an idiot. He refers to further cases published by Virchow, Schmincke, and others, and particularly to three cases of fatal carbon monoxide poisoning which died between the fourth and eleventh day, reported by Herzog, who found calcification in the vessels in the lenticular nucleus and mulberry-shaped bodies lying free in the supporting tissue. He considered that hyaline degeneration preceded the deposit of calcium salts in the vessels.

Dürch and Weingarten have both observed calcification in the vessels of the corpus striatum in cases of malignant malaria.

Weimann [18] has lately reported a case of dementia of ten years duration in which calcification was so widespread as to affect even the vessels in the pons.

The Pathogenesis of Calcification in the Cerebral Vessels.

The characteristic staining reaction with hæmatoxylin was accepted as sufficient evidence that the deposit occurring in the vessel walls and as globules consisted of calcium salts. No other specific stain for calcium was used.

Weimann has made an exhaustive chemical study of this deposit. He points out that in material which has been in formalin for any length of time most of the specific calcium tests are negative; he attributes this to the action of formic acid on the calcium. He further states that these deposits give a positive iron reaction, while tests for amyloid substance and glycogen were negative. He considers that the deposit is allied to a colloid group, and represents a ground substance containing iron and fatty substances. He emphasizes the fact that the deposit of the calcium granules first appears in the lymph spaces of the vessel wall, and he agrees with Hoefmeister who thinks that the deposition of calcium depends on an excess of calcium salts in the blood. The chalk is held in solution by protective colloids; if the latter be precipitated, then they may attract calcium salts, this process being further helped by a lowered CO_2 content of the blood.

Conclusions.

Although of considerable interest histologically I do not think that these changes play an important part in the production of the symptoms of paralysis agitans for the following reasons: (1) the lumina of the vessels remained patent except in one vessel in a single case. Despite this probable result I could find no evidence of serious nutritional alteration in the cells in the neighbourhood of the affected vessels or globules. (2) In two cases showing choreiform movements, i.e., Case 6, and a case of Huntington's chorea, well-marked calcification of the vessels in anterior part of the globus pallidus was found, but neither of these cases showed muscular rigidity or any evidence of alteration in the function of the large motor cells of the globus pallidus. (3) In Case 5, a chronic case of encephalitis lethargica, the chief clinical symptoms were involuntary movements; the degree of Parkinsonism in this case was extremely slight and may have been accounted for by the slight changes in the substantia nigra. On the other hand, the globus pallidus in this case showed a more advanced degree of calcification of vessels and more uncommon calcified globules than in any of the cases which presented the Parkinsonian syndrome in a marked degree.

Taking into consideration the facts mentioned by Weimann, and comparing the morbid process in encephalitis lethargica with that existing in those cases of carbon monoxide poisoning and malignant malaria in which calcification of vessels has been found, it seems evident that a toxic process, either of bacterial or gaseous origin, acts on the walls of the vessels and, either directly by causing a hyaline degeneration therein, or by so altering the tissue fluids circulating in the lymph spaces of the vessels that there is a modification in the normal state of the blood calcium, permits of a deposit of calcium salts within them. It seems probable that only this latter process could account for such a rapid deposit of calcium salts as has been shown to occur in acute cases of encephalitis lethargica. The selective action of the process on the vessels in the anterior portion of the globus pallidus I am unable to explain.

Summary.

An account is given of the histological findings in two cases of the Parkinsonian syndrome following encephalitis lethargica.

The most constant findings were subacute inflammatory changes and recent perivascular hæmorrhages. In one case the substantia nigra showed marked degenerative changes, and in the other this area appeared normal; but large hæmorrhages of arteriosclerotic origin in the basal ganglia considerably modify the negative findings in the substantia nigra in the second case. An account is given of fourteen similar cases reported in the literature, in all of which the substantia nigra was affected.

Calcification in the anterior part of the globus pallidus was found in six cases of encephalitis lethargica, in one case as early as the fourth day of the disease. The calcification was found both in the vessel walls and in the form of globules; the occurrence of fat globules was noted in one case, and the relation between these and the calcified globules was studied.

A short account is given of other conditions in which calcification occurs in the brain, and the pathogenesis and significance of these changes are discussed.

I must express my gratitude to Dr. J. G. Greenfield, Pathologist to the National Hospital for the Paralysed and Epileptic, Queen Square, London, for his valuable advice and great kindness in placing at my disposal a considerable amount of the morbid material which was used; also to Dr. J. P. Martin for permission to examine his sections from Case 5, and lastly to the various members of the staff of the National Hospital for permission to use and publish the notes of the cases which had been under their care.

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DESCRIPTION OF PLATE.

Camera lucida drawings of sections from the basal ganglia, showing various forms of calcification which affect the anterior half of the globus pallidus.

FIG. 1.—× 600. Diagrammatically arranged. (A) Case 4, Scharlach R. and hæmatoxylin; fat globules, showing pigmentary changes, and calcification in one globule. (B) and (C), Hæmatoxylin and van Gieson; larger forms of mulberry and calcified globules from various cases.

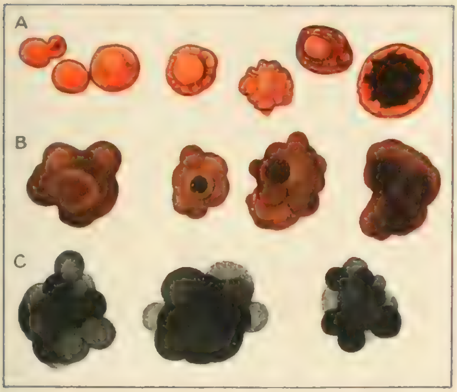
FIG. 2.—× 300. Case 4. Scharlach R. and hæmatoxylin. Fatty globules.

FIG. 3.—× 300. Case 3. Hæmatoxylin and van Gieson. Mulberry globules.

FIG. 4.—× 300. Case 5. Hæmatoxylin and van Gieson. Calcified globules.

FIG. 5.—× 250. Case 3. Hæmatoxylin and van Gieson. Early calcification in an artery.

FIG. 6.—× 250. Case 5. Hæmatoxylin and van Gieson. Calcification of vessels.



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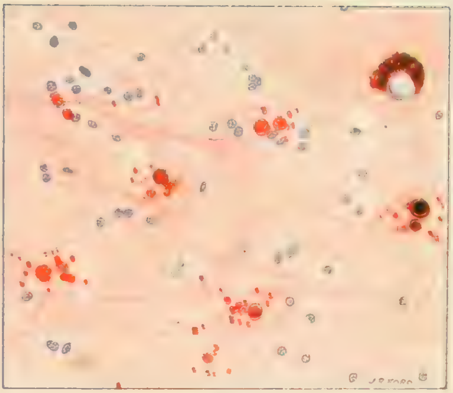

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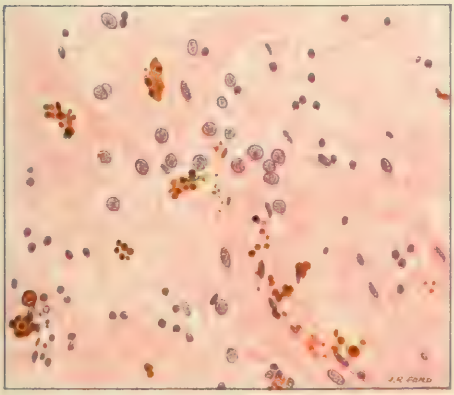

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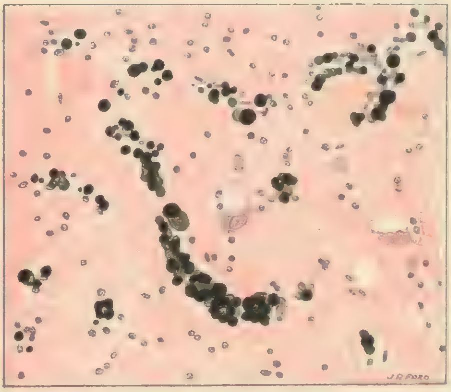

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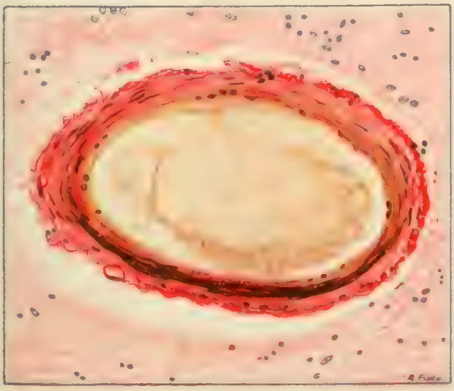

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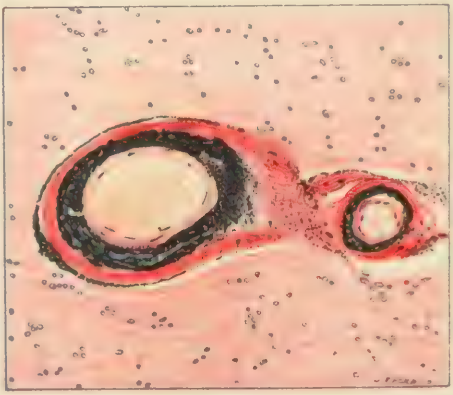

6.

ON VARIATIONS IN THE FORM OF REFLEX MOVEMENTS, NOTABLY THE BABINSKI PLANTAR RESPONSE, UNDER DIFFERENT DEGREES OF SPASTICITY AND UNDER THE INFLUENCE OF MAGNUS AND DE KLEIJN'S TONIC NECK REFLEX.

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Chapter I.—Introduction.

When the subject of a spastic residual hemiplegia firmly clenches the normal fist, the semiflexed and paralysed arm is seen to go into increased flexor hypertonus and to take up an attitude of increased flexion at the elbow until the voluntary grasp is relaxed, when it resumes its original posture and degree of spasticity. If now the patient be made to rotate his head towards the paralysed side and to repeat the experiment, it is found in many cases that the paralysed arm goes into tonic extension. In this simple observation we have an example of the modifying influence of one tonic reflex upon another, of a reflex arising in the proprioceptors of the neck upon one arising in those of the normal upper limb. In a recent paper [11], a series of tonic reflexes demonstrable in cases of hemiplegia was described and the study of their various modes of interaction led naturally to the question of interaction between postural and phasic reflexes, that is, between reflex postures and reflex movements. For example, is such a phasic reaction as the flexion reflex of the lower limb capable of modification in character under the influence of Magnus and de Kleijn's tonic neck reflex? Of particular interest is it to inquire whether the Babinski plantar response, which is a component of the flexion reflex, can be altered in form by changes in head posture. On the general question of interaction between tonic and phasic reflex reactions, the whole weight of experimental evidence indicates that the co-ordination of movement, both voluntary and reflex, demands a continuous and close co-operation of the two, either as reinforcing or as antagonistic reactions. Clinical investigation, also, has thrown some light upon the matter. For example, the experimental and clinical study of the knee-jerk, which is a simple phasic reflex, has shown that the presence or absence of tone in the reacting muscle materially modifies the form of the jerk: Viets [8]; Gordon Holmes [4]. The "shortening reaction" which is appended to the jerk when this occurs in a spastic muscle represents an element in co-ordination of the greatest importance. In a previous study of the effects of a loss of postural tone upon co-ordinated movement, we saw that the abolition of this "shortening reaction" is a prime factor in the production of the gross disorders of movement we speak of as cerebellar ataxy [10]. On the clinical side, however, there have been no observations as to the influence of tonic upon phasic reflexes when the relationship between the two is one of antagonism. If we take the flexion reflex of the lower limb as our example, we have to determine whether its form and time relations vary under different degrees of extensor spasticity in the leg. There are two ways in which we may investigate this: either we can take a series of cases of hemiplegia, or of spastic paraplegia in extension, in which there are different degrees of extensor spasticity, and compare the form of the flexion reflex in each; or a more precise way is to determine the effect upon the latter of Magnus and de Kleijn's tonic neck reflex. Here we can pit two different grades of extensor hypertonus against a single, constant flexion reflex. The first method presents no practical difficulty, but it is less easy to determine the influence of head posture upon the flexion reflex, either of the upper or the lower limb, for while in the latter we have a readily obtainable and extensively studied flexion reflex, it is only in relatively rare instances that we can demonstrate the influence of head posture upon the lower limb. In the upper limb, on the other hand, where it is the rule to find some degree of tonic reflex action upon the limb, it is exceptional to find the phasic flexion reflex described by Riddoch and Buzzard [5]. However, cases presenting reflexes of both types, the tonic neck reflexes and phasic flexion reflexes, in both upper and lower limbs have come under observation and it has been possible by this means to confirm the observations made by the method of comparison from subject to subject.

In an earlier paper [9] a full account of the flexion reflex of the lower limb in man has been given, and evidence advanced showing that the so-called "extensor" or Babinski type of plantar response is an integral part of this reaction. Subsequent work by Head and Riddoch [3] has confirmed this view. It is possible, therefore, to employ the Babinski plantar response as an index of variations in the flexion reflex under the influence of different degrees of antagonistic muscle tone; a fact which lends a certain practical significance to the observations about to be recorded.

CHAPTER II.—METHODS OF INVESTIGATION.

Some method of graphic recording is essential to a systematic study of the flexion reflex, more particularly of that part of it known as the "extensor" plantar response. While variations of the latter in form and duration may be visible to simple observation, no analysis of them is possible, nor can variations from moment to moment or from subject to subject be accurately compared apart from some permanent record of the movement. The method and the apparatus employed have been described in earlier papers [9, 11], and only a few remarks are here necessary.

The stimulus adopted is that commonly in use for eliciting the plantar response, namely, stroking of the outer margin of the sole with a blunt object, in this case a metal rod. A band of fine metallic gauze, such as is used in "ionization" treatment, is fastened round the foot and placed in circuit with an electric signal. The stimulating rod is similarly connected and its moment and duration of contact with the sole are thus recorded on the kymograph surface. The latent period obtained by this means is only approximately accurate, for it is the application of the stimulus which is recorded, and not the moment at which it becomes effective. However, the method is sufficiently accurate for the purpose in hand and gives a good record of the length of after-discharge of the reflex and of the moment of onset of "extensor rebound." In the case of the flexion reflex of the upper limb, since a momentary pinprick is the best form of stimulus, a more precise record of the latent period can be obtained, for the stimulating needle comes in contact with the metallic gauze covering the hand at the same moment as it pierces the skin.

CHAPTER III.—THE FLEXION REFLEX AND "EXTENSOR REBOUND."

When we compare the flexion reflex obtained on stimulation of the sole of the foot in a case of paraplegia in flexion with that obtained from one of spastic residual hemiplegia or of paraplegia in extension, certain differences in form and duration are at once apparent. In the former case, the whole limb goes into full flexion with considerable force, while the foot and digits dorsiflex. The active flexion outlasts the stimulus, which may be quite momentary, and finally the limb may retain the attitude of flexion thus reached, or may subside passively into its initial posture of partial flexion. In the second type of case, where the lower limb is spastic in extension, the salient feature of reflex is the dorsiflexion of the great toe, the Babinski type of plantar response. To such an extent is this true that only within the past ten years have neurologists come to associate the response with limb flexion. Nevertheless, even when there is no visible excursion of limb at hip and knee, palpation of the hamstring tendons reveals contraction of these muscles as an invariable accompaniment of the Babinski plantar response. Generally, however, there is some visible flexion at both hip and knee, but whatever its amplitude, the striking feature of this flexion of the limb is its transient duration and the quick and active return of the limb to the initial posture of extension.

If, then, we take the flexion reflex as a whole we find that the presence of extensor hypertonus diminishes its amplitude and cuts it short by a forceful and rapid return to the position of rest. In other words, the "after-discharge" characteristic of the unopposed flexion reflex is abolished by an "extensor rebound." If, on the other hand, we confine our attention to the dorsiflexion of the hallux, the effect of extensor hypertonus is much less striking, and requires for its appreciation the use of a graphic method. By this means, we find that the greater the degree of extensor hypertonus in the limb, the shorter the duration of the response; the shortening occurring on the return or extension phase.

The physiological principles underlying this influence of extensor hypertonus upon an intercurrent flexion reflex have been fully elucidated by Sherrington in the experimental animal, and his observations in this connection may be applied without qualification to the clinically observed phenomena. He says, "Many reflexes are intercurrent reactions, breaking in on a condition of neural equilibrium itself reflex. Take the case of the flexion reflex of the leg induced by a brief stimulus during "decerebrate rigidity," where the animal may be regarded as a bulbo-spinal machine . . . If, then, the foot be excited by a brief stimulus and thus a flexion reflex induced in the limb, the limb is drawn up at hip, knee and ankle. The movement is brief; after being drawn up, the limb returns to its previous pendent posture. It is easy in many instances to perceive that the pose of extension, as resumed, is more marked than it was prior to the intercurrent reflex of flexion. It is also equally easy to perceive that in the replacement of the limb the extension is not a mere passive drop under gravity, but is a reversion to the previous posture by an active movement . . . There is an *active* reflex return to the pre-existing pose . . . When the flexion reflex disturbed the neural equilibrium it dispossessed the opposed reflex of extension from certain final paths common to that and itself. In other words, its own reaction induces an after-coming reflex antagonistic to itself" [6]. Further, not only is reflex tonic extension restored, but it may be increased in intensity. This increase depends upon the fact that "the intercalated flexion reflex lowers the threshold for the after-coming extension reflexes . . . *during* the flexion reflex the extensor arcs were inhibited; *after* the flexion reflex these arcs are in this case evidently in a phase of exalted excitability" [6]. Sherrington speaks of this condition as "post-inhibitory exaltation." It is a phenomenon to which we shall have again to refer. The simple cutting short of the dorsiflexion component of the flexion reflex is not the only effect of the presence of extensor hypertonus in the limb. Not infrequently in those cases where ankle clonus is elicitable, stroking the sole of the foot elicits a dorsiflexion of the foot and toe followed at once, or accompanied, by a spontaneous ankle clonus which persists for from four to six seconds. The study of a series of graphic records shows that this clonus in some cases begins during the active dorsiflexion phase of the response, while in others it is not seen until the return or extension phase. There are two ways in which this phenomenon may be interpreted. Viets [8] has found that for the development of clonus there is an optimum grade of hypertonus, and that if by appropriate means extensor hypertonus be increased to this level a clonus will develop spontaneously. There are two ways in which extensor hypertonus may be increased when the flexion reflex is elicited. The active dorsiflexion of the foot suddenly increases the tension in the calf muscles, just as does the passive dorsiflexion employed in the normal method of eliciting clonus. Despite reciprocal inhibition, this sudden increase may bring the tone of the muscle to the level at which clonus is produced. This is probably the explanation in those cases in which the clonus begins on the active dorsiflexion phase of the reflex (fig. 5). The second explanation is that the extensor rebound, following the the active dorsiflexion and cutting it short, may be accompanied by the post-inhibitory exaltation referred to above, and that the hypertonus may

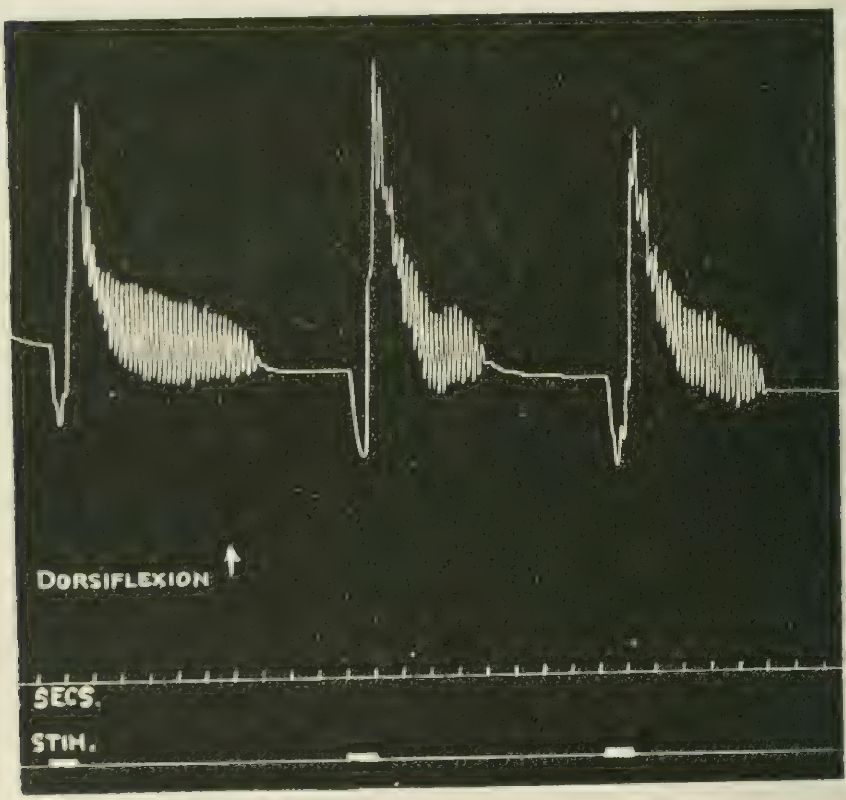

FIG. 1.—A series of three Babinski responses from a case of spastic paraplegia in extension (disseminated sclerosis). The dorsiflexion phase is preceded by a momentary plantarflexion. The extension or return phase of the response begins rapidly and during its course a spontaneous clonus develops. This lasts from four to six seconds and ceases with the foot and toe in the initial position of rest. In all figures, upward movement = dorsiflexion, and downward movement = plantarflexion. (1/1.)

in this way be brought to the optimum intensity for clonus. The cases in which clonus begins on the return or extension phase may possibly be explained in this way (figs. 1 and 2). In any case, whether or not the first explanation holds for both types, it is clear that the appearance of clonus is the result of a high degree of extensor hypertonus in the reacting limb and is a modification of the plantar response attributable to this cause.

In addition, these figures reveal another interesting feature of the plantar response, which has been already referred to in an earlier paper [9], and is not rarely seen when there is a high grade of extensor spasticity in the limb. It consists in a preliminary plantarflexion of the great toe, upon which the dorsiflexion follows immediately. Simultaneous records of hallux and limb movements indicate clearly that this plantarflexion also precedes the flexion at hip and knee. Babinski has quoted the occasional occurrence of plantarflexion of the great toe in association with reflex flexion of the limb in support of the thesis that the dorsiflexor plantar response is a reflex distinct and separable from the flexion reflex. As the records clearly indicate, the argument is illusory and serves but to show the necessity of graphic methods of investigation in the case of rapid reflex movements.

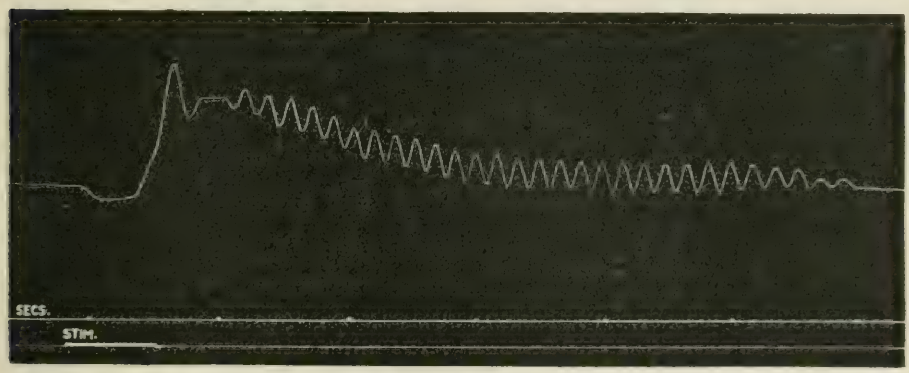

FIG. 2.—A similar record from the same patient taken on a rapidly moving surface. The development of clonus in the extension or return phase of the response is seen. (Reduced to 1/3.)

In a re-statement of his views on this point [1], Babinski has again referred to this phenomenon, and it is necessary, in consequence, to indicate anew its relation to the flexion reflex.

To summarize, we may say that taking the flexion reflex as a whole, the presence of hypertonus in the limb extensors profoundly alters the amplitude and duration of the reflex, so that the dorsiflexor component becomes the salient and sometimes the only visible feature of the reflex. It does this in virtue of extensor rebound. The dorsiflexor component is much less profoundly modified, partly on account of its inevitably smaller amplitude, and partly because its after-discharge is less prolonged even when the reflex as a whole is unopposed, than is that of flexion at hip and knee. Nevertheless, even this part of the reflex is cut short by rebound. In addition, the sudden tension in the calf muscles produced by the active dorsiflexion of the foot may set up a clonus, which is just visible during the active dorsiflexion phase of the response and reaches its full amplitude only when the rebound is established and the foot and toe are in active plantarflexion. In some cases, clonus appears only on the return phase, and may then be regarded as possibly a manifestation of post-inhibitory exaltation of the extensor hypertonus. Finally, the dorsiflexion of foot and toe may be preceded by a transient plantarflexion. Since the latter also precedes the flexion at hip and knee it affords no support to Babinski's contention that the plantarflexion is part of the flexion reflex and that the plantar response or dorsiflexion is a reflex distinct and separable from it.

CHAPTER IV.—THE FLEXION REFLEXES OF THE UPPER AND LOWER LIMBS AND THE TONIC NECK REFLEX: MODIFICATION OF THE BABINSKI PLANTAR RESPONSE ("REFLEX REVERSAL").

In the preceding chapter we have studied the effect upon the phasic flexion reflex of the lower limb of different degrees of extensor hypertonus. This necessitated the comparative study of the reflex in a series of cases. By means of Magnus and de Kleijn's tonic neck reflex we are able to produce variations in hypertonus in a single subject, at will, by the simple device of rotating his head towards or away from the hemiplegic side. It is true that so far as the lower limb is concerned we can do this in certain cases only, but, given a suitable subject, it is clear that we can examine the accuracy of the conclusions reached in the preceding chapter under very favourable conditions, for we are dealing with a constant flexion reflex which we can study against a background of at least two grades of antagonistic hypertonus. In short, the investigation of the influence of the tonic neck reflex upon the flexion reflex is simply an amplification of the observations already undertaken, and the results obtained are found to be strictly in accord with those described in the last chapter.

Figs. 3 and 4 record the dorsiflexion component of the flexion reflex (that is, the plantar response) in two cases of spastic residual hemiplegia in which the influence of the tonic neck reflex was just demonstrable in the leg. In each case, if the limb were supported by the observer while

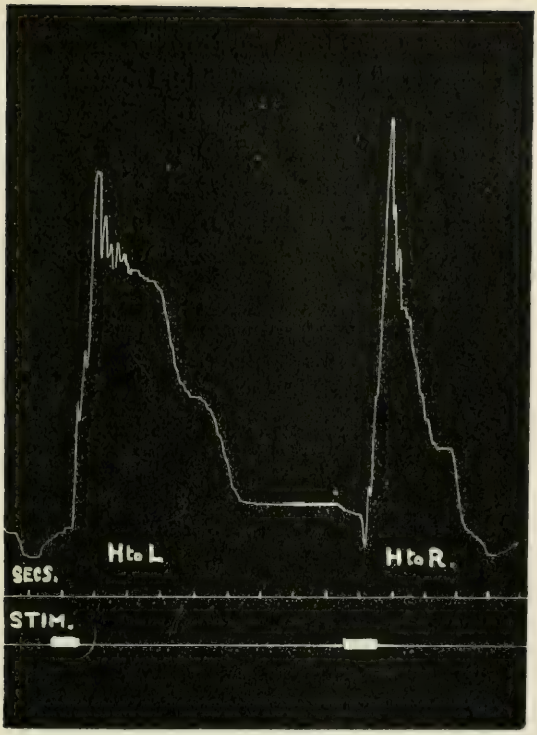

FIG. 3.—Two consecutive Babinski responses from a patient with right hemiplegia. With the head turned away from the paralysed side, the extension phase of the response is seen to be prolonged and the return to the initial position incomplete. With the head turned to the paralysed side, the extension phase of the response is appreciably shorter and the return complete. (1/1.)

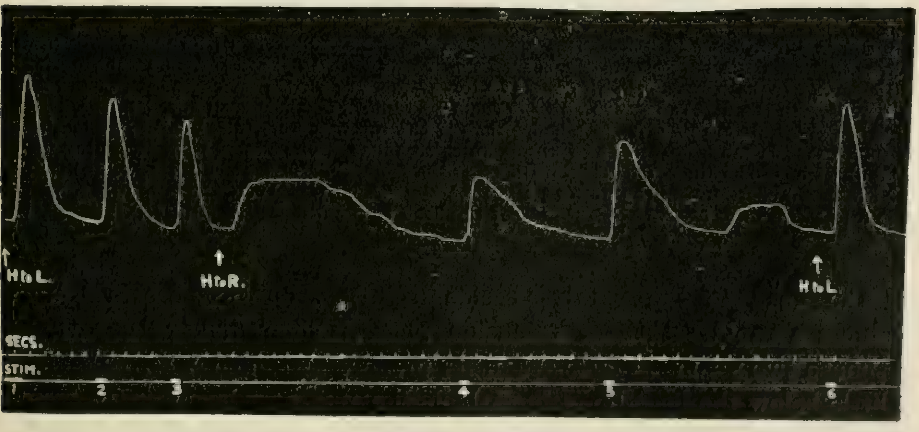

FIG. 4.—A series of seven consecutive Babinski responses from a patient with left hemiplegia. With the head rotated towards the left, the responses are cut short by extensor rebound (responses 1, 2, 3, 7). With the head rotated to the right the responses are strikingly prolonged in the extension or return phase (responses 4, 5, 6), and in the sixth response a second dorsiflexion occurs after the return to rest. (Reduced to 1/3.)

the patient voluntarily rotated his head through an angle of 180 degrees from the normal towards the paralysed side, it could be felt to become more spastic in extension. In fig. 3 are recorded two consecutive responses from one of these cases. The first was obtained with the subject's head rotated towards the normal side (left). It shows a leisurely relaxation or extension phase, which terminates a little short of return to the initial position. The second was obtained after rotation of the head to the paralysed side (right). Here extensor rebound induces a rapid return or extension phase, which makes the whole response two seconds shorter than its predecessors, and which reaches a little below the base line from which the response began. In fig. 4 is a series of seven consecutive responses from a case of left hemiplegia. With the head turned towards the normal (right) side, the return phase is notably longer than when the head is turned to the

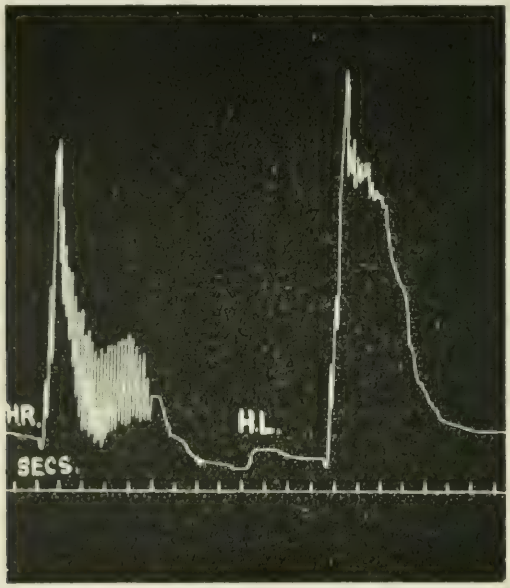

FIG. 5.—Two consecutive plantar responses. The first obtained with the subject's head turned towards the hemiplegic (right) side, the second with the head turned to the normal (left) side. In both responses two beats of the clonus are visible on the active dorsiflexor upstroke. In the first the return phase is rapid and clonus reaches a full development. The foot and toe return to a level just below that of the original base line. In the second, the return phase is more leisurely and is not quite complete. The clonus is minimal in range and duration. The difference between the two records depends upon the diminished intensity of extensor hypertonus of the limb at the time the second was taken, the diminution being the result of a tonic neck reflex (rotation of the head to the normal side). (1/1.)

affected (left) side, the difference being a matter of several seconds. In this series, the prolonged responses were less ample than the shorter ones, but this finding was not invariable for this or other subjects. In a third case, the plantar response was accompanied by ankle clonus, which made its appearance during the active dorsiflexion movement, but reached its full development only during the return or plantarflexion phase. With the subject's head rotated towards the hemiplegic (right) side, an ample clonus is seen during the extension (plantarflexion) phase, but with the head turned towards the normal (left) side, the dorsiflexion is more ample, the return is delayed and the clonus is minimal. (Fig. 5.)

In two patients in whom well-developed tonic neck reflexes were present in both upper and lower limbs, even more striking modifications of reflex movements were demonstrable.

R. S., a seaman, aged 27, was admitted to hospital with a history of having received a blow on the right side of the head two years previously. He had been rendered unconscious, in which condition he had been trephined in the right parieto-occipital region. Both injury and operation occurred in Antwerp and no details of either are available. His present state (March, 1923) is that he has a spastic left hemiplegia of some severity. The arm is held flexed and adducted and retains relatively little voluntary power. He walks with extended leg and drags the foot. There is complete left homonymous hemianopia, but no impairment of acuity for any form of sensation. There is, however, a marked emotional overaction to painful stimuli applied to the left half of the body, and in the case of the arm a brisk flexion reflex accompanies pin prick or pinching (*vide infra*). The left tendon jerks are very brisk, there is ankle clonus on this side, the left abdominal reflexes are absent, and the left plantar is of the Babinski type, with slight rapid flexion at hip and knee. The spasticity of the left limbs is marked. Certain reflex reactions in the affected limbs may now be described at greater length.

Tonic neck reflexes.—With the patient lying on his back, rotation of the head to the normal side is followed by a slightly increased flexion posture of the arm (which is slung) and by slight active flexion of the supported leg, both of which are tonically maintained. Rotation of the head to the paralysed (left) side is followed by very slight extension of the arm due to diminution of the pre-existent degree of flexor hypertonus, and by increased extensor hypertonus in the leg.

Tonic neck reflexes and associated reaction.—On grasping with the normal hand, the following reactions are observed: Head in centre = flexion adduction of the arm. Head to left = extension-abduction of the arm. Head to right = flexion of the arm. A corresponding but less forceful and ample reaction is observed in the hemiplegic leg.

Phasic flexion reflex of the upper limb (*left*).—Pricking or pinching of the skin of the upper limb anywhere below the level of the insertion of deltoid, or of the skin covering pectoralis major and the axilla, gives a brisk movement of flexion-adduction of the limb. The latency of this is 0·04 second. The response is the same in form from whatever part of the receptive field it is elicited.

Phasic flexion reflex of upper limb and tonic neck reflex.—The response described above is obtained with the patient lying on his back, the head in the median position and the arm slung. With the head to the right (normal) side, the flexion is more marked and the forearm and hand shoot across the body towards the right shoulder. If the head be now rotated to the affected (left) side, *the response is reversed in form*, and becomes one of extension-abduction of the limb. The latency is unchanged, but the distinct and constant tonic prolongation and shortening reaction of the original flexion reflex are both lacking. These differences in direction and form are readily apparent in figs. 6 and 7, which were taken on different days, but still show the same essential features.

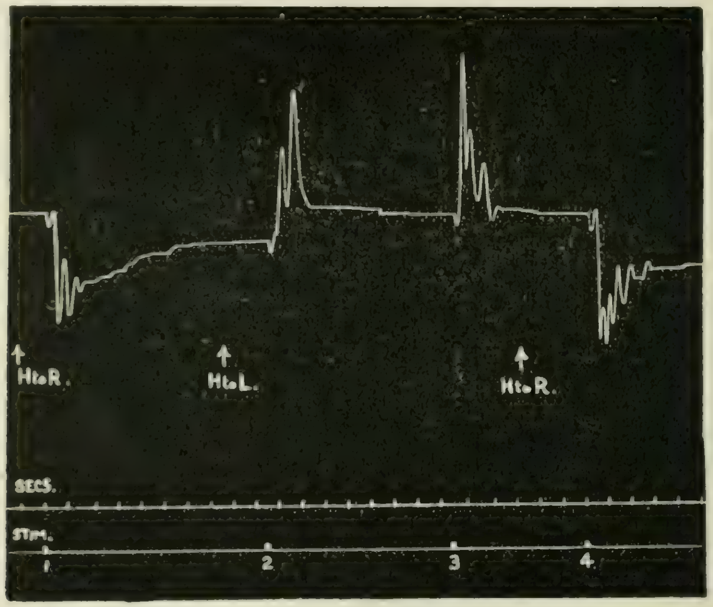

FIG. 6.—A series of four reflex movements from the upper limb in a case of left hemiplegia. The first and fourth consist in a flexion-adduction movement, that is, a movement employing the spastic flexors of the limb, and show marked tonic prolongation and shortening reaction. They were obtained with the head rotated to the right (normal) side. The second and third reflexes were obtained with the head rotated to the left (hemiplegic) side, and consist in a rapid movement of extension-abduction of the limb, without shortening reaction or tonic prolongation. The striking difference between the two types of response can be seen by looking at the record upside down. Down movement = flexion. Upward movement = extension. (Reduced to 2/3.)

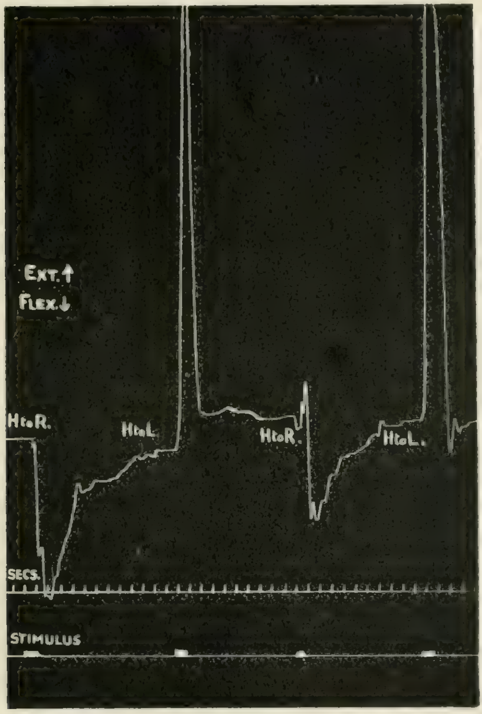

Fig. 7.—A similar record obtained from the same patient on another occasion. (Reduced to 2/3.)

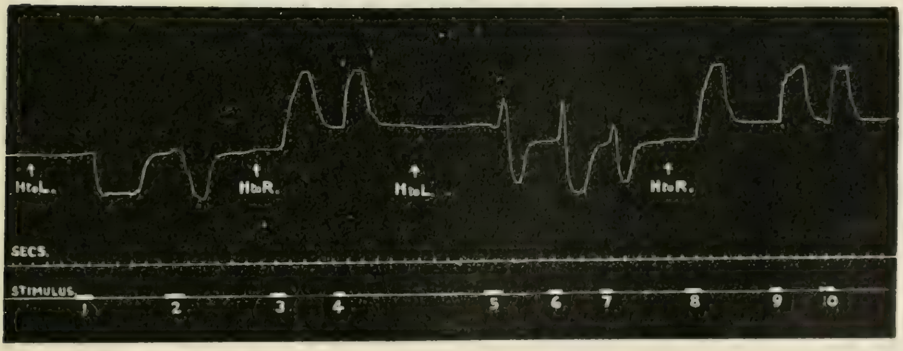

Fig. 8.—A series of plantar responses obtained with the head in the two lateral positions (Patient R. S.); 1, 2, 5, 6, 7, with the head turned towards the hemiplegic (left) side, and 3, 4, 8, 9, 10, with the head turned away from the hemiplegic side. The first two responses are completely plantarflexion, but the fifth, sixth, and seventh show an initial, diminished and very short-lived dorsiflexion (Babinski) response. Figs. 5, 6, and 7 were obtained from the same patient. (Reduced to 1/3.)

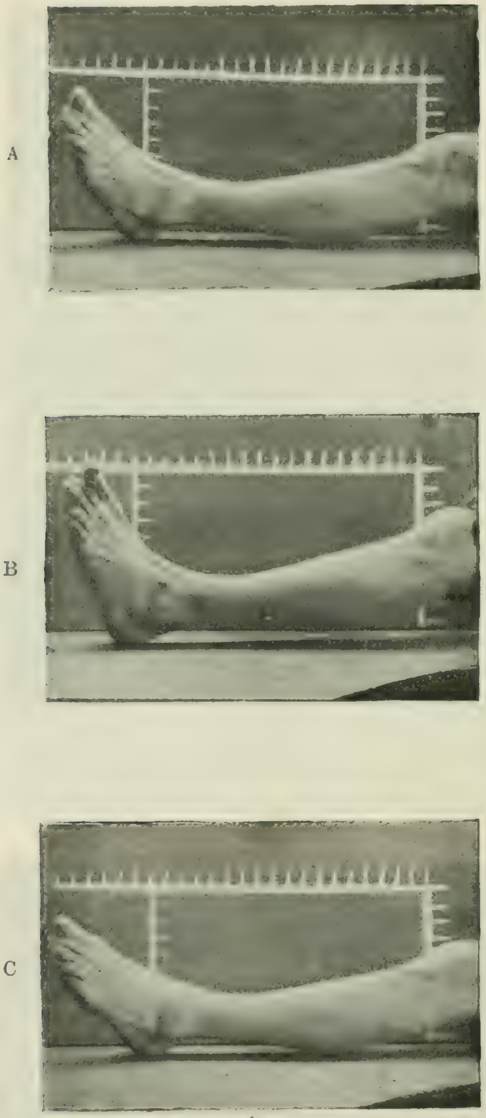

Fig. 9, A, B, C.—Three photographs from the patient R. S. A = the resting position of the left leg. B = the response to stimulation of the sole with the head rotated to the right. It consists of slight flexion at hip and knee with dorsiflexion of the foot and toe. C = the response to stimulation of the sole with the head rotated to the left (hemiplegic) side. This consists of a transient initial dorsiflexion of the hallux followed by active plantar-flexion of the foot and hallux, which is the phase here represented.

The scale marked on the background is in inches, and indicates the amplitude of the various movements.

This observation is of considerable physiological interest. By means of the tonic neck reflex the phenomenon of "reflex reversal" has been elicited, and as a result the relationship of phasic to tonic reflex changes from one of reinforcement (in the flexion reflex) to one of antagonism (in the extension-abduction reflex), with modifications in the form of the response which are visible in the records.

Flexion reflex of the lower limb and tonic neck reflex.—With the patient on his back and head rotated to the right (normal) side, the response to stroking the sole is a rapid slight flexion at hip and knee, the latter being lifted about three inches from the surface of the couch, and ample dorsiflexion of the foot and great toe. The average duration of the plantar component is three seconds. With the head rotated to the left (hemiplegic) side, the whole flexion reflex is altered. There is no visible flexion at hip or knee, and the plantar component consists of an extremely rapid and short-lived dorsiflexion of the great toe, lasting 0·8 second, and followed at once by ample plantarflexion of the foot and great toe. With mild degrees of stimulation there may be no initial dorsiflexion, uncomplicated plantarflexion occurring. However, increase in the strength of the stimulus always brings out the rapid, small dorsiflexion of the hallux. This finding was constant throughout a large series of examinations carried out over a period of several months (figs. 8 and 9).

A similar modification of the flexion reflex of the lower limb under the influence of changes in head posture was observed in a patient with a left hemiplegia, the subject of a cerebral tumour in the region of the third ventricle.

F. D., a woman, aged 24, was admitted to hospital with a six months' history of slight headache and occasional vomiting, and seven days' history of blindness of sudden onset. The patient was completely blind in both eyes from papillœdema and early secondary atrophy. No localizing signs were discovered. Following a right-sided decompression above the tentorium, she gradually lapsed into profound stupor and developed a left hemiplegia. In the course of two weeks, this became spastic and showed the characteristic attitude of the affected limbs and the usual reflex phenomena. In these circumstances, as the patient lay on her back in bed in a semi-conscious state, passive rotation of the head evoked well-marked tonic neck reflexes in both arm and leg. Rotation of the head to the left (hemiplegic) side was followed by active and maintained extension of the arm, and also of the leg if this were previously held in semiflexion by the observer. However, when the leg was already in extension, a marked plantarflexion of the foot followed and was maintained as long as the head remained turned to the left. *The flexion reflex of the lower limb* with the head rotated to the right (normal) side, consisted in slight flexion at hip and knee, with slow ample dorsiflexion of the foot and hallux. After the stimulus had ceased, the return to rest was incomplete, but if the head were now rotated to the left the foot and toe at once returned to their initial posture. With the head turned to the left (hemiplegic) side, the flexion at hip and knee was much less ample, while the dorsiflexor component of the reflex was much shorter in duration, slightly reduced in amplitude, and was cut short by a quick extensor rebound. A series of these responses is seen in fig. 10. The modification produced by head rotation to the hemiplegic side is slightly different in character from that noted in the patient R.S., but is not less striking.

Several points of interest emerge from these observations. In respect of the flexion reflex of the upper limb, we see that the direction of a reflex movement may be reversed by a concurrent tonic reflex. Rotation of the subject's head towards the hemiplegic side tends to diminish the hypertonus of the limb flexors, so that now stimulation of the skin of the limb produces a reflex movement of extension. This "*reflex reversal*" is an example of a condition described by Graham Brown in the decerebrate animal, as resulting from the active assumption of a new posture by the reacting limb, and comes within the scope of the rule which he has formulated that "a stimulus which may throw into activity either of twin antagonistic centres (and depress the activity of the other) will tend to activate that which at the time is already in a state of relatively raised activity" [2]. More recently,

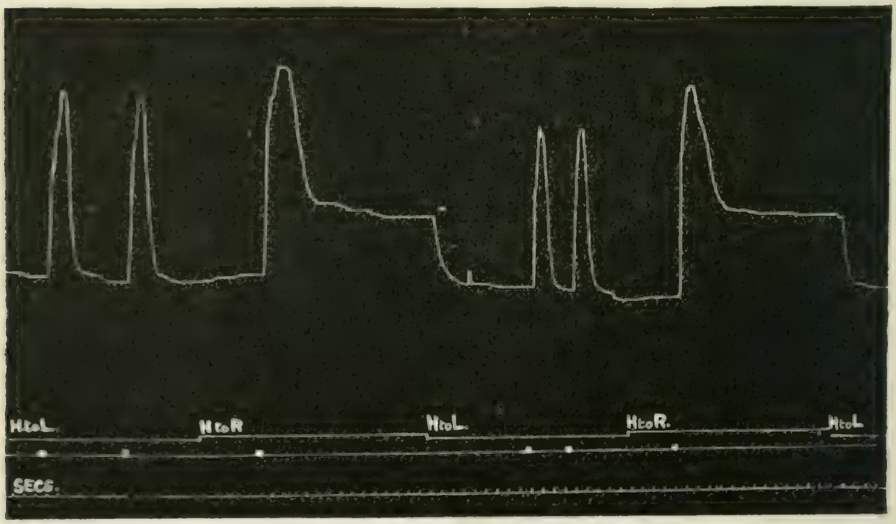

FIG. 10.—A series of six consecutive plantar responses from a case of left hemiplegia (Case F. D.) : 1, 2, 4, and 5 were obtained with the head turned towards the (hemiplegic) left side; 3 and 6 with the head turned towards the (normal) right side. In the two latter the extension or return phase is prolonged and incomplete, but rotation of the head to the left (see upper signal) is at once followed by an active extension (plantarflexion) of foot and great toe to the initial position. (Reduced to 1/2.)

Socin and Storm van Leeuwen [7] have also described similar examples of reflex reversal in the decerebrate animal under the influence of Magnus and de Kleijn's tonic reflexes.

In the case of the lower limb, in the subject R.S. (Case 1) there is a similar but less pronounced tendency to reflex reversal, for with the head rotated towards the hemiplegic side the dorsiflexion component of the flexion reflex is seen to be constantly reduced in amplitude and duration, sometimes to be completely abolished, a plantarflexion (that is, an extension reflex movement) either cutting dorsiflexion short or replacing it.

It is interesting to recall that in their cases of reflex movement of the upper limb in hemiplegia, Riddoch and Buzzard found that in every subject but one the response was one of flexion. In the exception, extension was observed. Whether head posture played any part in the latter is an interesting matter for conjecture.

We may summarize the results described in this chapter as follows: In the case of the flexion reflexes of both upper and lower limbs, the active modification of the posture of the reacting limb by the tonic neck reflex tends to reverse the form of the reflex. In the case of the upper limb, this "reflex reversal" may be complete, but as seen in the lower limb it is incomplete and leads to diminution of amplitude and duration of the reflex. From the clinical point of view, we may express this tendency to reversal in respect of the Babinski plantar response and say that in certain cases of hemiplegia rotation of the head towards the affected side of the body alters the form of this response, and may even lead to its disappearance unless strong stimulation of the sole is employed.

In the case of the reversal of the flexion reflex of the upper limb, we have an example of a reflex movement employing muscles already engaged in a tonic reflex (flexor spasticity) being changed to one employing the antagonists of the spastic muscles (the extensors). In this way the relation of the two reflex reactions—phasic and tonic—is altered from one of reinforcement to one of antagonism. As a result the character of the reflex movement changes in the manner visible in the graphic records.

CHAPTER V.—CONCLUSIONS.

The observations recorded here raise several points of interest in the physiology of the nervous system, and demonstrate the essential similarity of the nervous processes governing the co-ordination of movements of posture in man and the lower animals. In a previous paper we have seen that of the different tonic reflexes obtainable in certain cases of hemiplegia, one may profoundly influence the form of another which is synchronous with it. Thus, the associated flexion of the paralysed arm evoked by firm clenching of the normal hand may be converted into associated extension by a tonic neck reflex, produced by rotation of the subject's head towards the hemiplegic side. The present paper records observations made to determine whether certain of the reflex movements obtainable in man in spastic paralysis are also capable of modification by tonic reactions of this kind. The relationship of a tonic to a phasic reflex, i.e., of a reflex posture to a reflex movement, may be that of reinforcement or of antagonism. Clinically, the tonic prolongation of the knee-jerk in spastic paralysis is a familiar example of the former, but of the latter no examples have been precisely studied in man, although in animals Sherrington and others have analysed the result of such an antagonism. Clinically, the problem is readily investigated, for in the flexion reflex and the extensor spasticity of the lower limb we have a phasic and a tonic reflex respectively, employing antagonistic muscle groups—the flexors and dorsiflexors in the first case, and the extensors and plantarflexors in the second. We may, therefore, compare the form of the flexion reflex in a series of subjects with different grades of extensor spasticity in the limb. We may also study the flexion reflex in a single subject with the head in each of the two lateral positions (rotation to right and to left), that is, we may study it against a background of at least two grades of hypertonus. Further, since the Babinski type of plantar response is an integral part of the flexion reflex, of which it is the dorsiflexion component, we may use it as an index of variations in the form of the reflex. The main results of these observations may be expressed as follows: the presence of a high grade of extensor hypertonus reduces the amplitude and duration of the hip and knee flexion components of the flexion reflex very considerably. The Babinski plantar response component is less influenced, so that it may become the salient feature of the reaction. Nevertheless, this is also modified, particularly by the shortening of its duration. This cutting short and reduction of the flexion reflex is due to "extensor rebound," the nature of which is discussed. There may, however, be other manifestations than these. For example, the active dorsiflexion of the foot in the flexion reflex may, by the sudden increase of tension induced in the calf muscles, give rise to ankle clonus. In some cases the clonus makes its appearance during the active dorsiflexion, but does not reach its full development as long as the flexion reflex is in possession of the limb musculature. On the return of the extension phase, however, a full and ample clonus develops and lasts for some four to six seconds. In other cases, the clonus does not appear until the return phase is in progress. It is possible that here another factor is responsible. Rebound is known to be accompanied by an increased excitability, a "post-inhibitory exaltation" in the spasticity which has been transiently overset by the flexion reflex. This exaltation may, at certain levels of hypertonus, lead to the development of clonus in the manner described by Viets. Moreover, the marked depression of this clonus resulting from rotation of the head towards the normal side, as seen in fig. 5, shows that although tension on the calf muscles may be the stimulus producing clonus, yet the intensity of rebound is a further factor of importance. Probably both factors are at work in every case of clonus elicited in these circumstances. In those cases in which head rotation influences the degree of extensor tone in the lower limb, the same laws are seen to obtain, and in addition we may get an actual "reflex reversal" on stimulating the sole from the altered state of tone induced by the tonic neck reflex. When this reversal is not in question, rotation of the head towards the hemiplegic side increases hypertonus and thus leads to shortening of the Babinski component of the flexion reflex. Rotation of the head to the normal side lessens it and thus the response is appreciably lengthened. The lengthening occurs on the return phase and is due to a diminished intensity of extensor rebound. In those cases where clonus occurs in association with the plantar response, rotation of the head to the normal side may lead to its diminution almost to the point of extinction. One example of reflex reversal of the Babinski component of the flexion reflex is described. Here the dorsiflexion of foot and great toe is cut short before it reaches its full height and is at once followed by a slow and ample plantarflexion of both. To mild degrees of stimulation, the Babinski component may fail altogether, simple plantarflexion being the sole response.

One example of flexion reflex of the upper limb (Riddoch and Buzzard) came under observation, and here the influence of head rotation towards the paralysed side was completely to reverse the form of the reflex movement, changing it from one of flexion-adduction of the limb to one of extension-abduction. The circumstances in which this occurred and the principle underlying the change are those defined by Graham Brown as governing "reflex reversal" from the assumption of a new active posture by the reacting limb. Another point of interest exemplified by this reversal is that in the reflex movement of flexion the spastic flexors were the prime movers and, therefore, the two types of reflex were allied in their activity. The reflex extension on the other hand employed the non-spastic extensors of the limb and, therefore, stood to the tonic reflex (flexor spasticity) in the relation of an antagonistic reflex. The modification in the character of the movement resulting from this alteration of relation is seen in the graphic records.

Finally, a practical point emerges, namely, that the Babinski type of plantar response may be diminished, or even abolished, by rotation of the head to the paralysed side of the body in hemiplegia. How often this phenomenon may be demonstrable, it remains for further experience to decide, but that it can occur at all suggests that it may be worth while, in cases where the plantar response is equivocal in form, to rotate the subject's head towards the opposite side when attempting to elicit the Babinski response.

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ON CEREBELLAR LOCALIZATION.

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A FEW years ago the writer, in a study principally devoted to the phylogenetic and ontogenetic development of the cerebellum [16], undertook to review the literature on the functions of the cerebellum and the localization of function within it. Anatomical and physiological considerations in connection with my own studies, and also with those of predecessors, induced me to put forth some principles concerning both the function of the cerebellum and the localization of the function in this organ. Since then several authors have discussed these same problems, and it has also become possible to consult works that were not available to me during the war. The following pages are intended as a further review of the progress made in these questions during the last few years. Two cases of cerebellar lesion that I have had the opportunity of observing in the Clinic of Internal Medicine, Lund University, will be used as a basis for this discussion. I take this occasion to extend to Professor Karl Petrén, as the head of this department, my thanks for his courtesy in giving me the chance of examining these cases.

Our knowledge of the cerebellum culminates in a few very important facts, all of which indicate that a great fundamental and uniform function is represented in this organ. The cerebellar cortex differs from the cerebral in showing no differences of histological structure. This statement means not only that all animals have the same layers of cells in the cerebellar cortex but also that the structure is the same in all parts of the cortex, even in the most intricate cerebellum, the human.

The second great principle in favour of this thesis is the fact that the cerebellum is built up in the same manner in all animals. Bolk has demonstrated this in mammals. In a study of cerebellar phylogenesis the writer was able to collect evidence to show that the cerebellum is constructed according to the same laws in the whole series of vertebrates

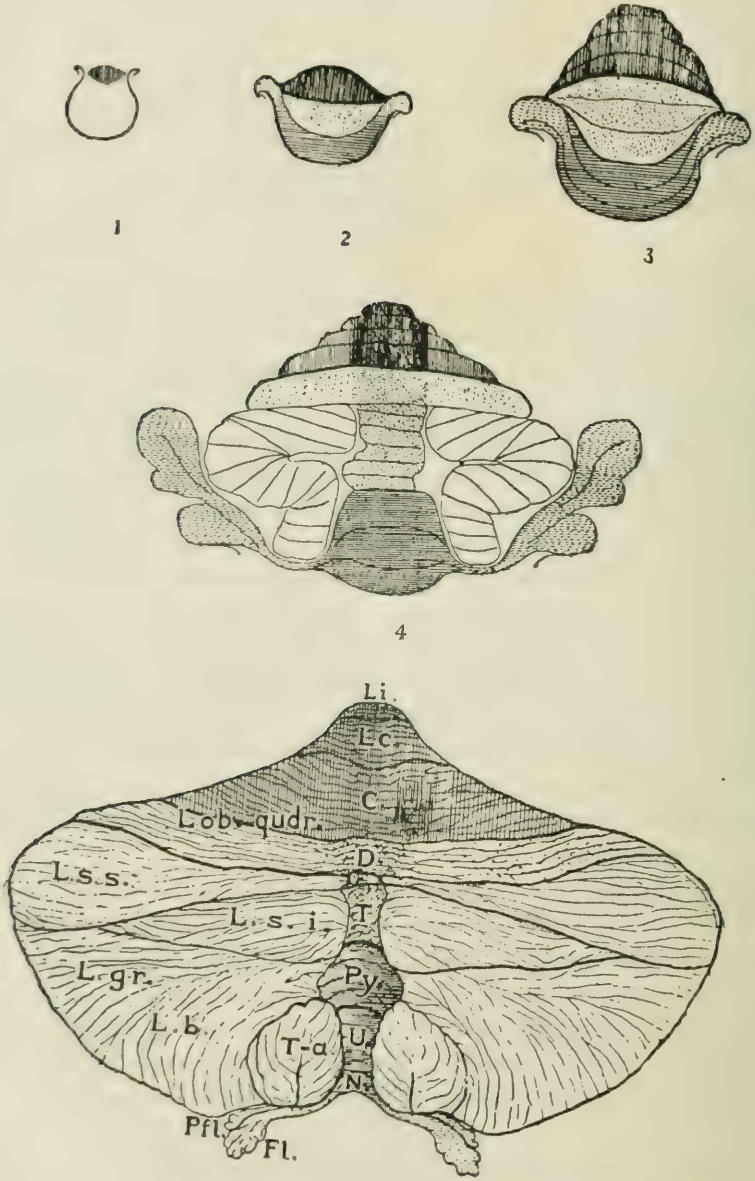

FIG. 1.—Diagrams of the cerebellum of (1) lacerta; (2) alligator; (3) bird; (4) mammal; (5) man; showing the homologies in the cerebellums of all these vertebrate classes. Vertical lines: lobus anterior. Horizontal lines and stipplings: lobus posterior. White area: lobus medius.

(fig. 1). The bony fishes cannot be included in this statement, because their development in this as in other respects seems to have gone its own way, but in the rest of the vertebrate series there seems to be a complete homology between the different parts of the organ, from the lowest to the highest. Thus, for instance, the alligator already has the same principal parts of the cerebellum as man.

The third great principle is that in all vertebrates without exception the cerebellum develops in the same place of the neuraxis. It cannot be a mere chance that the cerebellum always appears above the vestibular nerves. In lower vertebrates, such as petromyzon, it is a simple layer of cortical structure lying directly on the medullary nuclei of the eighth nerve, while in mammals fibres run directly from Scarpa's vestibular ganglion to the basal parts of its cortex. Thus the intimate relations of the cerebellum to the labyrinth are obvious.

Naturally, all these facts indicate a uniform function in all animals, and a uniform function in all parts of the cerebellar cortex, but they do not exclude a localization of function. As will be developed more fully below, there is a strong argument for localization in the distribution of the afferent fibres to the organ, since the different afferent tracts are distributed to different cortical regions. Such an arrangement must undoubtedly mean that in different regions different functions are localized. It must be assumed that the cortical function of a special region is brought into play only or mainly from a certain region of the body, and that the function irradiates from a certain area in the cerebellar cortex by the way of anatomical pathways only or mainly to special parts of the body. Thus we are not without anatomical indications of localization, even though they are scanty compared with the evidences of localization in the cerebral cortex.

The credit of the first important contribution to our knowledge of cerebellar localization must undoubtedly be given to the Dutch anatomist, Bolk. He was the first to study exhaustively the comparative anatomy of the mammalian cerebellum and to analyse its structure, which was a necessary preliminary to the investigation of localization within it.

Bolk divided the cerebellum into two parts, the lobus anterior and the lobus posterior, separated by a deep fissure, the sulcus primarius, which is a very conspicuous feature in all animals. The architecture of the lobus anterior is relatively simple and constant. The larger posterior part, owing to its more complicated structure, is also called lobulus complicatus. Its lateral parts, which form the lobulus anso-paramedianus, show the greatest variations.

The present writer (16) has found it necessary to criticize this subdivision of the organ into two parts. In my comparative studies of the cerebellum of all vertebrates I found an interesting parallelism between the most anterior and the most posterior parts of the organ. I therefore considered it necessary to divide the organ into *three parts*, a lobus anterior with the same limits as Bolk's anterior lobe, a lobus posterior, and between them a lobus medius.

It is necessary to emphasize in general terms the importance of this subdivision of the organ into at least three parts. No homogeneous sensory area in the nervous system ever develops by means of marginal appositions ; the differentiation always takes place in the centre. The inferior olive, for instance, is in lower mammals a more or less plane disk, but as development places greater demands on its function it expands into a folded structure which reaches its highest development in the human brain. Even here its oldest parts are still those situated around the hilus, which would, if the olive were spread out in one plane, represent its periphery. That these parts are really the oldest from a phylogenetic point of view is indicated by the fact that in certain degenerative processes of the cerebellum, where the phylogenetically younger regions particularly suffer, all parts of the olive are affected except those around the hilus (Brouwer) [7]. Several other examples could be mentioned to prove this assertion. In this connection, it should not be forgotten that the same principle is found also in the architecture of the cerebral hemisphere. In lower vertebrates (frogs and alligators) this is related to the olfactory nerve and serves mainly as a centre for the sense of smell, and if the human hemisphere were spread in one plane it would be found that the whole area is bordered by the hippocampus, gyrus fornicatus, &c., that is, by the rhinencephalon. All anatomists (Kappers, Vogt, Brodmann, &c.) agree that these cortical areas are the oldest parts of the hemisphere. Within this original frame the magnificent vaulting of the hemisphere expands during the development. Next to the rhinencephalon, the cortical areas of the different senses are the oldest parts, and so far as their localization is known, we find them in the immediate neighbourhood of the cortex of rhinencephalon, the area striata or the visual area around the fissura calcarina, and the small gyri transversi or the auditory centre in the fissure of Sylvius (Flechsig, Henschen). In other words they also are situated in the borders of the hemisphere, and between them centres for the higher psychical functions appear. This is the general formula for the development and differentiation of the cerebral hemisphere, as well as of every so-called sensory area of the nervous system.

The cerebellar cortex, with its uniform histological structure in all vertebrates, develops according to the same principles. In my comparative studies I found many signs that its marginal regions, that is the regions situated at the base of the organ immediately above the fourth ventricle, are the oldest parts from a phylogenetic point of view. They vary little during development, and their phylogenetic differentiation is very limited. They take no part in the intricate expansion found in higher mammals, the culmination of which is the building up of the human cerebellar hemispheres.

It is therefore necessary to consider the central parts of the cerebellar cortex separate from the border areas. As the cortex develops in an antero-posterior direction it will be necessary to divide the organ, from this point of view, into at least three parts, following each other from before backwards.

The anterior lobe must be given the same boundaries as described by Bolk. It forms the greatest part of the anterior vermis rostral to sulcus primarius. To the middle lobe belong mainly the two lobi ansoparamediani, i.e., the largest parts of the hemispheres. The posterior lobe consists of the most posterior segment of the vermis (pyramis, uvula and nodulus) and the floccular formations (flocculus and paraflocculus).

Therefore the limit between the middle and the posterior lobe is the sulcus præ-pyramidalis. I cannot recapitulate here all the arguments for the choosing of this borderline; I may only mention that it is indicated by certain characteristic features on the exterior of the organ. In many mammals (sheep and horse for instance) all lamellæ behind sulcus præ-pyramidalis have a much coarser architecture than the medial lamellæ lying in front of this fissure, indicating that the parts behind it must be regarded as a morphological unit in relation to the parts in front of it.

A study of the fibre connections of the cerebellum gives further support to the subdivision of the organ into three parts. The spinocerebellar fibres, which reach the cerebellum by way of the tracts of Flechsig and Gowers, end almost exclusively in the anterior and the posterior lobes, whereas the middle lobe receives none. The termination of these fibres was at first studied by Horsley and Salusbury MacNalty [12], but, as I have pointed out in my first contribution on the cerebellum [16], it is difficult to get a clear idea from this work of the cortical regions where they terminate. My own experimental studies on dogs and pigeons showed that the middle lobe is almost free from spinocerebellar fibres.

Bremer [6] has recently corroborated this statement. By exciting the cerebellar cortex in cats with weak electric currents, he found two cortical areas from which inhibition of the extension of the extremities could be elicited. Bremer writes: " The excitable zone has very distinct boundaries. In the anterior vermis it does not exceed the middle of the central lobe. The posterior boundary runs about one or two millimetres from the primary fissure. Another inhibitory area is found at the level of pyramis. These areas correspond exactly with the two regions where Ingvar has found that the spino-cerebellar tracts end."

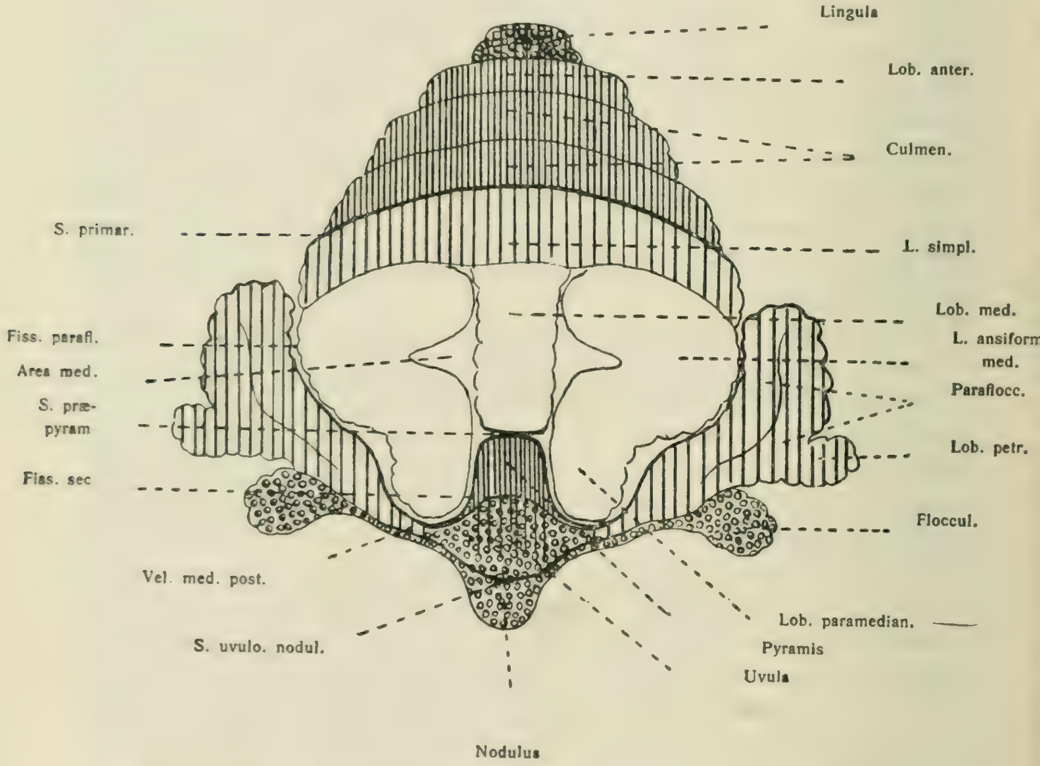

FIG. 2.—Diagram of the mammalian cerebellum, the cortex being spread into one plane. Vertical lines mark the endings of the spino-cerebellar tracts; circles mark endings of direct fibres from the vestibular nerves. The surface of the cerebellar cortex is conceived of as being spread in one plane; the periphery of the figure corresponds to the base of the organ, that is, those parts situated in the immediate vicinity of the fourth ventricle and especially of the vestibular nuclei.

The fact that anatomical and physiological evidence here agree is significant. We undoubtedly have in these two spinally innervated areas two fixed starting points for the further study of cerebellar localization.

Comolli and Edinger introduced the terms palæo-cerebellum and neo-cerebellum to indicate the different phylogenetic age of different regions of the organ. The oldest region, according to these authors, is the entire vermis and the flocculi, which they consequently termed the palæo-cerebellum. The rest of the organ, comprising the hemispheres and the lateral parts of the anterior lobe, was included in the neo-cerebellum. I have found it necessary to oppose this manner of subdivision, since many facts indicate that the vermis is not a morphological entity, and Bremer's physiological findings have corroborated this view. He has suggested that the anterior and posterior lobes (mihi) should be together called the palæo-cerebellum, and that the lobus medius (mihi) be designated the neo-cerebellum. I think this use of the significative and expressive terms is a happy one, and expresses the phylogenetic history of the organ more accurately than the system of Edinger and Comolli.

Marie, Foix and Alajouanine [24] are wrong in accusing me of having entirely rejected the conception of Edinger and Comolli of the palæo- and neo-cerebellum. I have only shown that it is not correct to regard the vermis as an anatomical and functional unit, running through the organ in a sagittal direction.

My subdivision of the cerebellum into three main lobes has been adopted by Kappers, Ransom, Bremer, and Marburg. I emphasize this point because of its great importance in the question of localization. It is impossible to have any idea of the functions of an organ until we have some knowledge of its structure. That experimental work on localization has failed to afford conclusive evidence is due to a large extent to the fact that the operators did not know, or did not pay attention to, the morphological subdivision of the organ. Parts considered as units have been excised which later investigations have shown to belong to different entities.

All these considerations cannot fail to have a great influence on our conception of the function of, and localization in, the cerebellum. In fact they form a most important key for a clear understanding of these important and difficult problems.

In considering the function of the middle lobe it is advisable to start with a consideration of our general knowledge of this region of the cerebellum. The middle lobe is built up of the parts called by Bolk the lobuli ansiformis and paramedianus. These were shown by my own anatomical studies to appear first in mammals. They must be accordingly considered as the specific mammalian component of the cerebellum. They appear contemporaneously with the pons and the pyramidal tracts. The pontine fibres to the cerebellum are mainly connected with this middle lobe, and as the development of the pyramidal tract means a higher differentiation of motility, the development of the middle lobe of the cerebellum must also be related to regulation of the highest and youngest motor functions of mammals.

It is in these parts that a regional representation of the different sections of the body has been demonstrated. Bolk concluded from his anatomical studies that the lobi ansiformis and paramedianus must be functionally related to the activities of the extremities. He inferred that the anterior part of the ansiform lobe (*crus primum*) is related to the anterior extremity, while its posterior region, called *crus secundum*, has the same relation to the hind limb. His anatomical studies were succeeded by a long series of experimental observations by van Rhyneberk, Luna, Rossi, Lussana, Rothmann, Marrassini, Thomas, Durupt and Galante among others, all of which have confirmed his views of the arrangement of the centres for the anterior and posterior limbs in mammals.

It must be mentioned that Hesser and Troell [11] have raised doubts on this localization. They were unable to find evidence of any regional representation either within the middle lobe or in the whole cerebellum. After lesions of the anterior crus they found symptoms in the posterior limb and vice versa. Rossi, who must be considered as one of the most experienced workers on cerebellar physiology, has after a critical discussion of the symptoms following lesions in the middle lobe, concluded that there must be at least a prevalence of representation. In other words the fore-limb is related mainly but not exclusively to the anterior crus and the hind-limb mainly to the posterior crus and the paramedian lobe.

Altogether, almost all authors agree that the lateral parts of lobus medius, i.e., the hemispheres, are in functional relation with the extremities. So far the question of localization in the cerebellum seems to be settled.

There is no such agreement about the functions of the anterior and posterior lobes, but anatomical knowledge afforded by my studies has not failed to give valuable hints.

It seems reasonable to conclude that these parts, which have changed so little during phylogenetic development, have a fundamental function. Furthermore, the fact that these lobes receive the spino-cerebellar fibres, which originate from all segments of the spinal cord (Bing, Marburg) and are not segmentally represented in the cerebellar cortex, makes it highly probable that these regions have a function correlated to all spinal segments, that is the body or organism as a whole. But still more the fact that the anterior and posterior lobes receive fibres belonging to the vestibular nerves points in the same direction.

The most anterior parts of the anterior lobe and the most caudal parts of the posterior lobe are located in immediate vicinity to each other at the base of cerebellum and in proximity to the vestibular nuclei. That this is not accidental is shown by the fact that to these basal lamellæ (the lingula of the anterior lobe and the uvula, nodulus and flocculus of the posterior lobe) direct fibres go from the vestibular ganglia. I was able to show this experimentally by means of the Marchi method in the brain of a congenitally deaf cat, in which the vestibular nerve had been cut [16].

Valuable support is afforded to this view by the experimental observations of Greggio. After excision of the vestibular peripheral organs in new-born pigeons, he found a defective development of the cerebellum, particularly of its most posterior parts, that is of its basal lamellæ. Mesdag has in his ontogenetic studies of the brain of the fowl clearly demonstrated how vestibular fibres run only to the most posterior parts of the cerebellum.

These direct vestibular fibres suggest very strongly intimate vestibular relations of the basal regions of the cerebellum. A study of the functions of the peripheral vestibular organ and of the vestibular nerve may give us further insight into the possible function of these parts.

Of all the cerebellopetal fibres there are undoubtedly none of which the function is so well known as the vestibulo-cerebellar. The most prominent feature in the anatomy of the peripheral vestibular organs is the arrangement of the semicircular canals in the three planes of space. We also know that the clinical symptomatology of vestibular lesions is, as it were, connected with the different planes of space. Thus we find a lesion of the horizontal canal results in nystagmus which is mainly horizontal, past-pointing of the extremities in the horizontal plane, and lateropulsion of the body (Bárány). Any disturbance of a vertical canal produces vertical nystagmus, past-pointing in the vertical plane (upwards or downwards), and a tendency to fall backwards or forwards, that is in the same vertical plane as the irritated canal. *There must be therefore a grouping of vestibular impulses in the central nervous system in relation to these planes.* Otherwise it would be impossible to explain the fact that the irritation of a vertical canal, for instance, produces vertical nystagmus, vertical past-pointing, and falling in the same plane. The vestibular impressions, acting on the mesencephalic motor apparatus for the eyes, as well as on the spinal motor apparatus for the extremities and the trunk, are grouped in relation to the planes of space, and this must necessarily also hold for the vestibular influence on the cerebellum. The vestibular innervation of the cerebellar cortex must therefore be arranged on the principle of the different planes of space. A similar view has been previously adopted by several authors (Ferrier, Hughlings Jackson). There are also, in fact, a few clinical observations which indicate that this is the case. Léri [23] concludes that each semicircular canal must be connected with a special region of the cerebellar cortex (compare p. 320).

This point of view also suggests that the functions of the cerebellum must in some way be related to the different planes of space. Many authors have studied symptoms of cerebellar disease from this aspect; Bárány has shown that certain deficiency symptoms due to cerebellar lesions, as past-pointing, are limited to certain planes, and the experimental observations of Thomas and Durupt show that the same principle holds in animals. It is an old observation that the falling in cerebellar lesions is mostly in one special direction, backwards, forwards, or to one side. The direction varies in different cases, but it is often constant in the same case during the whole period of the illness. From these facts it seems highly probable that the innervation of the cerebellum is related to the action of different synergic groups of muscles acting in one special direction, or in one plane of space.

It seems logical to expect such symptoms to result from disease of those parts of the cerebellar cortex that are innervated directly from the vestibular nerve. A lesion of these regions can to a certain extent be considered as a lesion of the vestibular nerve itself. In fact, after lesions of these parts very characteristic symptoms appear in the acute stage, the so-called forced movements which in many respects remind one of pure vestibular symptoms.

We know from physiological experiments that after lesions of the lateral parts of the cerebellum there appear certain motor phenomena known as "forced movements"; the animal falls towards the side of lesion, that is rotates around its own axis. This phenomenon increases as the lateral peduncles are the more involved in the lesion. There is no agreement on the direction of falling, except that in the majority of the cases it is towards the side of the lesion, but it also occurs towards the opposite side. A tendency to fall forwards or backwards following lateral lesions is very seldom observed.

Forced movements in the sagittal plane, around a frontal axis of the body, are, on the other hand, a prominent feature after lesions of the medial part, i.e., the so-called vermis of the cerebellum.

In animals total experimental destruction of these medial regions offers great difficulties. The most anterior part of the vermis is situated in the cavity beneath the cerebellum, immediately above the fourth ventricle, and any attempt to remove the whole anterior lobe therefore involves the risk of injuring the medulla oblongata also. In fact a study of the majority of the records of operations on the lobus anterior shows that only its upper or more or less superficial parts had been damaged. The lobus posterior is more easily removed, but its most caudal part, the nodulus, is located very deeply, and it is only when special attention is paid to it that it can be extirpated with the rest of the lobus posterior. From our knowledge of the connections of the basal lamellæ it is evident that these parts must have very important functions. But as a rule these lamellæ are spared in experiments, owing to technical difficulties, and this may be the reason for many obscure and contradictory statements concerning forced movements in the experimental literature. For this reason also the work of Hesser and Troell [11] is hardly apt to give any elucidation of the question of the origin and the direction of forced movements in the sagittal plane, because these parts were not removed in any animal recorded by these authors.

In my studies on the basal parts of the cerebellum, I found that when the posterior lobe had been totally removed the animals showed a remarkable tendency to fall backwards, whereas in animals in which the anterior lobe had been removed quite other symptoms were observed. I therefore concluded that the synergies necessary for maintaining the body balance backwards were regulated in this part of the cerebellum.

A tendency to fall backwards has been observed by several operators on the cerebellum (Ferrier, Marrassini, Thomas and Rothmann), but there is no agreement as to the injury of which parts this phenomenon was due; some observers observed this symptom after lesions of lobus anterior. Russell [32] found that his animals fell backwards after ablation of pyramis, declivum and part of the monticulus. Rotation movements were not observed in such animals, except in one instance when they occurred a few hours after operation and then were slight. When the greater part of the vermis, including the whole of the posterior half and some of the anterior, was extirpated, the tendency to fall backwards was slighter than when the posterior portion of this lobe alone was removed.

My own studies [16] confirmed Russell's results entirely. Recently Simonelli [33] has investigated this same question. In order to test my results he has removed in dogs, cats and rabbits, the posterior lobe, as I have described it. He summarized his results in the following manner: "After ablation of the posterior lobe there are to be seen dynamic phenomena of a mainly accessory type. They are characterized by dorsal extension of the head, extension of the anterior extremities, opisthotonos, falling backwards and crises of motor agitation." Only when the uvula and nodulus were removed did falling backwards appear. Lesions of the pyramis gave no such symptoms. From this it will be seen that the symptoms observed by Simonelli are the same as those described in my work, and so far I consider that this author has corroborated my observations. Simonelli, however, regards the backward falling of the animals as a so-called dynamic phenomenon, not as a deficiency symptom (compare p. 313). However, it must be considered as absolutely proven that after ablation of the most posterior parts of the cerebellum (the nodulus and the uvula) there appear in different animals immediately after the lesion motor phenomena characterized by a falling backwards. From no other part of the cerebellum can this phenomenon be elicited in the same manner.

From my own experiments and also from those of Simonelli it is clear that the falling backwards is most prominent when the uvula and nodulus are entirely destroyed. The fact that the falling backwards is elicited especially from those parts innervated by the vestibular nerve makes it very probable that the vestibular innervation plays some rôle in this phenomenon. This assumption is all the more probable since this falling backwards is very similar to that which appears after lesions of the vertical semicircular canal.

Simonelli has criticized my theory of cerebellar localization. In spite of the fact that he has found the same phenomena in his operated animals, he concludes that the posterior lobe has nothing to do with the falling backwards of the body. This paradox depends on Simonelli's interpretation of the falling backwards as a so-called *dynamic* symptom. Luciani was the first who termed these acute motor phenomena which follow cerebellar lesions, i.e., the forced movements, dynamic. He concluded that they cannot be considered as genuine symptoms of cerebellar deficiency, but should be regarded as secondary in some way to vertiginous paroxysms due to irritation or paralysis of the cerebellar peduncles.

Simonelli expressly states that the falling backwards observed in his animals was certainly due directly to the cerebellar lesion. The fact that this phenomenon only persisted during the first days after the operation induces him to call it "accessory." And as a true adherent of Luciani he considers that it is without importance in our interpretation of the function of the posterior lobe.

It is clear without further discussion how arbitrary such an interpretation is. How is it possible to denounce the value of a symptom that is of cerebellar origin? It seems to me that Simonelli here has sacrificed too much to his loyalty to his great countryman. The fact that the dynamic phenomena appear only in the acute stage of the lesion does not entitle us to put them aside as valueless in the study of the cerebellar physiology. As it has been proven that destructions of the posterior lobe elicit most typically symptoms of falling backwards, we must ascribe to the posterior lobe the faculty of eliciting in some way the necessary muscular synergies that are necessary to bring about the falling backwards, even if this symptom persists only during the acute stage, and even if we do not know the reason why it disappears. We cannot afford to put them aside as valueless, as accessory. The difference of opinion between Simonelli and myself is thus merely a matter of interpretation.

As the dynamic phenomena seem to be more severe after injuries to those parts that are directly influenced by the vestibular nerve, these regions would seem promising ones for future study. The uniformity of the cerebellar cortex makes it highly probable that the organization of the function in all parts of the cerebellar cortex is identical. Thus if we are able to reveal the organization of the function of the basal parts we will have a key to an understanding of the whole cerebellum.

The experiments of Magnus and de Kleijn [22] on the relation of the vestibular organs to the attitude of the body and its different parts have shown that all these reactions (Stellungsreflexe, vestibular reflexes) persist after the removal of the cerebellum. Their conclusion is that the cerebellum can no longer be considered as the main organ of the vestibular nerve, as it has been in both anatomical and physiological

logical literature (Sherrington). Their observations do not refute what has been said above; they merely show that the reflex mechanism of body-attitude which is related to the vestibular apparatus is laid down in the medulla, mid-brain and spinal cord, as it were underneath the cerebellum. These authors leave the question open whether in an intact central nervous system vestibular impulses reach the cerebellum and take part in its function. The fact that Scarpa's ganglion sends fibres directly to the cerebellar cortex is too strong an argument in favour of the vestibular influence on the cerebellum to be neglected. Though great caution must be exercised in translating anatomical facts into physiological theories, if structure means anything we must insist upon the functional relationship between the vestibular nerves and the cerebellum. The work of Magnus and de Kleijn shows that the importance of vestibular influence on cerebellar function must not be overestimated, as there has been a tendency to do in both the anatomical and the physiological literature.

The cerebellum may be considered as a conglomerate of nervous tissue where impulses from different sources are correlated. The two most important sources of these impulses are undoubtedly the vestibular organs and the spino-cerebellar paths, but other cranial sensory nerves also contribute.

During phylogenesis there has been a tendency to regression of the vestibular organs and to further development of the spino-cerebellar pathways. Many signs indicate that the vestibular organs constitute a sense organ fitted for orientation in a fluid or gaseous medium (water and air); a dog from whom they have been removed will drown if thrown into water, but if the cerebellum only is removed he can swim. Human beings without a functioning vestibular apparatus never learn to swim. Fishes and birds have comparatively much greater peripheral vestibular organs than mammals, and especially than the higher animals. On the other hand the spino-cerebellar tracts increase in size during phylogenesis; fishes have spino-cerebellar fibres from the cervical segments only (Kappers), whereas in mammals they come also from the lowest segments of the cord (Bing, Marburg).

There are, therefore, grounds for the theory that during phylogenesis the influence of the labyrinth on the cerebellum diminishes, while that of the spino-cerebellar tract increases. Consequently, if impulses reaching the cerebellum from the exterior by the only two possible ways, vestibulo- and spino-cerebellar tracts, are elaborated here, the spino-cerebellar influences ought to play a more important part than the vestibular in higher animals. This is in accordance with the findings and conclusions of Magnus and de Kleijn.

The theory of vestibular function now most generally accepted is that formulated by Mach, Breuer and Crum Brown, according to which the static and kinetic properties of the endolymph and the otoliths are the active stimuli of the peripheral vestibular apparatus. Since, according to this interpretation, the vestibular nerve conducts impulses initiated by static and kinetic changes in the vestibular organ, it is impulses of this nature that reach the basal regions of the cerebellum to which the vestibular fibres run directly.

This is in complete accordance with the old conception, first formulated by Magendie, of the cerebellum as an organ for the regulation of the equilibrium of the body. This function naturally cannot be limited to the static equilibrium of the body; it must also during motion regulate the different muscular activities concerned in dynamic equilibrium. I have, in my anatomical studies, declared myself an adherent of the view that the cerebellum is a reflex organ which preserves the static and dynamic equilibrium of the organism. This conception receives the strongest theoretical and logical support from the great uniform principles in the constitution of the cerebellum mentioned in the introduction to this article. It is in accordance with the anatomical and phylogenetical relations of the cerebellum and the vestibular nerves, and with our knowledge of the functions of the labyrinth. It explains better than any other hypothesis the great anatomical and histological uniformity of the cerebellum in the whole vertebrate series. It is also in accordance with the clinical symptoms of cerebellar disease.

As an organ regulating the static and dynamic equilibrium of the body masses it must, as I have pointed out [16], regulate muscle tone in the different regions of the body in all muscular activities. In 1918 I tried to interpret all the various clinical cerebellar symptoms as a disturbance of muscular tone, and to give a consistent explanation of cerebellar syndromes. So far as I know I was the first in this endeavour. Later Ramsay Hunt [15] and especially Walshe [38] and Holmes [14], have given explanations of the cerebellar symptoms, that in important parts are identical to mine and in other respects come very close to it. On the whole, it can be said that there has in later years been a general tendency in the literature to abandon the conception of Luciani, who divided cerebellar symptoms into atonic, astenic and astatic components. Even the Italian school has tried to consider the cerebellar syndromes from a more uniform point of view. So Rossi and Simonelli

[30] explain the astatic and most of the so-called astenic symptoms as a consequence of the atonia. There has since 1918 been a growing tendency to attempt a uniform explanation of all cerebellar symptoms and attribute them to a disturbance of one specific function. By many authors the cerebellum has been looked upon as the reflex organ for the co-ordination of the muscular activities. Gordon Holmes writes: "A fuller recognition of the part that the postural tone plays in both active and passive attitudes and in the movement has cut down enormously the symptoms in the explanation of which it is necessary to invoke incoordination."

Bolk concluded from his anatomical studies that the anterior lobe was related to the muscular functions of the head (the face, tongue, larynx, &c.), whereas the posterior lobe (mihi) was related to those of the trunk, and especially of the tail and perineum. My studies on the fibre connections make one doubtful about this system of localization. The fibre connections of the anterior and posterior lobes indicate strongly that the functions of these parts must be related to the body as a whole and not to any special segment of it.

I concluded further that the anterior lobe was related mainly to regulating the motor functions necessary to maintain the equilibrium of the body and preventing the body from falling forwards, whereas the posterior lobe played a rôle in maintaining the equilibrium backwards.

It is interesting to find that Gordon Holmes in his recent extensive studies on the clinical symptomatology of cerebellar lesions writes: "Certain facts indicate that there may be a further localization of function within the human vermis; I have for example observed a tendency to stagger backwards in tumours and other lesions of its posterior portion, and a falling forwards in one case at least of tumour in its anterior part."

According to this there is no regional representation of the body segments within the cerebellar cortex of the anterior and posterior lobes. That which is localized here is the complex of different synergies acting in equilibrium, according to the principle of the direction in the different spacial planes. In these parts the regulation of the synergies necessary for the static and dynamic equilibrium of the body as a whole is laid down.

The same principles can be applied to the middle lobe. Here it seems to be definitely proved that the anterior region (crus anterius) is related to the activities of the fore-limb, whereas the posterior part (crus secundum) is related to the posterior limb. But also here the conception of the cerebellum as a regulating organ of muscular tone, in order to preserve and maintain the static and dynamic equilibrium of the body masses, is a strong objection against any definite regional representation of different body segments in its cortex. Only a prevalence of representation in the sense of Rossi would be in accordance with the above principles.

In later times several observations have been made that have been interpreted as unfavourable to all theories of localization. So Rossi [29] has stimulated the cerebellar cortex with electrical currents and thereby found that the excitability of the contralateral cerebral motor cortex is increased. If one point of the latter is selected, for instance that which gives flexion of the arm, its excitability can be equally modified from several points of the cerebellar cortex. Beck and Bikeles [4, 5] have studied the electrical variations of the cerebellar cortex after stimulation of the cerebral motor cortex. They were not able to detect any local correspondence between the latter and the cerebellum. Miller and Banting [26] have shown that electrical stimulation of a certain point of the anterior lobe inhibits decerebrate rigidity in both homolateral limbs and excites bilateral movements.

These observations, however, cannot be used as objections to the system of localization which has been developed in the above pages. The conception of the cerebellum as an organ for the reflex adjustment of static and dynamic equilibrium involves necessarily the idea of a widespread representation in the cerebellar cortex of almost all motor activities. All movements, even of the most peripheral parts of the extremities, imply activities of fixation of the trunk musculature and the joints proximal to that which is interested in the action. Noica [27] has demonstrated how cerebellar disturbances diminish or disappear in the extremities if the proximal joints are fixed passively during the movements.

It is therefore not surprising to find that cerebellar lesions generally produce widespread symptoms. But especially we have to expect the most severe symptoms in lesions of the anterior and posterior lobes. My own experiments showed that lesions of these parts really result in severe disturbances. Simonelli [34] states the removal of the posterior lobe produces a very grave disturbance of all the motor functions of the animal. The experiments of Weed, and of Banting and Milner [26], according to which electrical stimulation of the anterior lobe elicits manifestations in the whole body, inhibition of the decerebrate rigidity &c., are also in accordance with this.

The above pages have been mainly concerned with the knowledge of the anatomy and physiology of the cerebellum acquired from studies on animals.

Hitherto the endeavour to apply knowledge acquired by experimental studies in animals to clinical phenomena have not been quite successful. It must be here emphasized that the human cerebellum is built according to the same principles as the mammalian cerebellum.

In the highest mammals (the anthropoids) and in man the lobuli ansiformes and paramediani develop into the huge hemispheres that are so characteristic of the cerebellum in these species. There is, according to my anatomical studies, no reason to suppose there exists in the human cerebellum any specific new parts, such as would make it different from others; the part that seems to have especially developed in it is the biventral lobe. This may be related to the specific demands that the erect gait places upon the motor functions of the lower extremities. Accordingly, we should expect to find here the specific leg centre; this assumption agrees entirely with the observations made in the first case described below.

Another conspicuous difference between the cerebellum of man and that of other mammals is that the paraflocculus—the large formation found laterally in all mammals—has undergone regression in man and exists only as the tiny accessory flocculus (Henle). This may be related to the fact that, owing to the erect gait, the trigeminal region has not the same importance in motility in man as it has in quadrupeds, where it is a very important organ for grasping, defence, &c. But, for the rest, there is a complete homology between the lobi ansiformis and paramedianus in mammals and those parts in the human cerebellum extending from and including the lobulus semilunaris superior, to and including the tonsils.

Accordingly anatomical facts indicate that the function of, and localization in, the human cerebellum must be organized in the same way as in the mammalian cerebellum. If the knowledge of the cerebellum acquired from experimental physiology is applied to the clinical symptomatology of cerebellar diseases we immediately will find interesting agreements.

We have above pointed out that the fact that direct vestibular fibres and all the spino-cerebellar fibres run only to the anterior and posterior lobes, indicates that these parts are functionally related to the whole body. This is in accordance with clinical observations. The anterior and posterior lobes form the palæocerebellum, and of this the vermis constitutes a large part. There seems to be a general agreement that lesions of these parts produce symptoms affecting the whole body, mainly disturbances of the equilibrium, a staggering gait and falling. This is not in contradiction with the assumption of a special centre in the cerebellar cortex for the leg, as will be shown later. If it is the function of the basal parts of the cerebellum to regulate the equilibrium of the body, they must, of course, especially in man and the anthropoids, influence the motor activities of the lower extremities. Hence the principal effect of disease of the palæocerebellum in man is disturbances in the legs (staggering gait, &c.).

A tendency to falling in vermis lesions is often mentioned in the clinical literature; Nothnagel refers to it and states that it usually occurs in a forward or backward direction. Adler [1], Bruns [8], Stewart and Holmes [35], have reported several cases. According to some authors, a lesion in the posterior part of the cerebellum produces falling backwards, and a lesion in the anterior portion falling forwards (Holmes [14]), but on the whole it must be said that there is no general agreement about the direction of the falling. When the lateral parts of the cerebellum are affected the patient falls sideways, either to the same side or to the opposite. The clinical literature thus affords strong evidence that a lesion of the vermis produces falling in a more or less sagittal direction, whereas a lesion of the hemispheres causes falling in a lateral direction. So far, clinical observations are in accordance with the principles of localization that have been discussed in this article.

It must be said that human pathology has offered only slight evidence of a functional localization within the middle lobe. Nevertheless there are a few clinical observations that strongly speak in its favour and tend to corroborate Bolk's conclusions on the localization of function in the most recent parts of the cerebellar hemisphere, which correspond to the mammalian lobulus ansiformis. André Thomas states that the centres of the arm and leg in the human cerebellum are arranged in the same manner as in cats and dogs, the anterior part of lobulus ansiformis being related to the arm and the posterior to the leg. That the arm is related to the anterior part of lobus ansiformis is shown by a case of cerebellar abscess described by Thomas, in which the symptoms were limited to the right arm, though the serious condition of the patient did not permit a careful examination. After death an abscess was found in the substance of the right superior semilunar lobe, but the whole hemisphere seems to have suffered, since it was œdematous and more voluminous than the left. The fact that the symptoms affected principally the arm gives a certain importance to this case. It speaks in favour of an arm centre in the lobus semilunaris superior.

In his recent publication [36] Thomas gives several instances of cerebellar lesions where the symptoms appeared mainly in the upper or the lower limb. Such observations indicate that there must be a strict localization of these regions of the body in the cerebellum. Unfortunately, the author had no opportunity of correlating his clinical observations with the anatomical lesions and these cases have, therefore, only a restricted importance.

Rothmann mentions a case in which he was able to diagnose an otogenic cerebellar abscess in "the posterior part of the hemisphere," owing to the fact that the ataxia had started in the leg. Marburg finds that tumours of the ponto-cerebellar angle produce more marked symptoms in the arm than in the leg. The first observation of cerebellar disturbances limited to the leg, in which clinical observation had been strictly confirmed by the autopsy, was my first case described in the following pages. It was first published in 1919 [20] and is strongly in favour of this physiological system of localization in the human cerebellum.

Léri [23] published a very important observation in 1917. A soldier, aged 31, was wounded in the neck by a bullet which had penetrated from behind and was found under the occipital protuberance in a relatively superficial position, from which it was easily extracted. There were two wounds, one corresponding to the upper or middle part of the inferior vermis, the other to the left hemisphere. From the rapid regression of the symptoms the author concluded there was a superficial lesion of the cerebellum. Two or three months after the injury this patient had obvious symptoms of cerebellar deficiency, *but in the legs only*; the arms were unaffected. On changing the position of the head in an antero-posterior plane only, the patient developed vertigo. The trembling of the legs also appeared only in an antero-posterior direction. The author draws the following very important conclusions: "There is in man in the inferior vermis a centre in charge of the coordination of the motility of the legs. An even superficial lesion here gives symptoms exclusively localized in the inferior extremities (*parasyndrome cérébellaire*)." Furthermore, the author concludes that there must be definite relation between each semicircular canal and special cortical areas in cerebellum from the fact that the vertigo in his case could be elicited only by movements of the head in an antero-posterior direction.

The value of this case is limited by the fact that the site of the lesion was not verified. It is, of course, impossible to form any exact idea of its real extent, but in view of the symptoms I am inclined to locate it somewhat more caudally than the author does. Anyhow, the inferior surface of the cerebellum was certainly injured.

In other respects also this case is exceedingly interesting. Thus the tremor in the antero-posterior plane, and the fact that vertigo was produced by movements of the head in this plane only, agree in a remarkable way with conceptions developed in this article (compare p. 310) .They will later be discussed.

Gordon Holmes [14] writes (p. 115) : " My observations do not lend support to the theory of circumscribed functional representation of different parts of the body in the lateral lobes." A small lesion, according to this author, usually produces symptoms equally from the arm and the leg. But further the author writes : " In a certain number of cases, however, the one limb seemed to be relatively more affected than the other, the leg being more involved by caudal and mesial lesions and the arm by the more anterior. It is possible, then, that there is a " prevalence of representation " in the Rossi sense, the arm being represented more anteriorly and the leg more posteriorly, but this localization is so indefinite that I would not regard it as a trustworthy guide in the diagnosis of a small lesion, such as a cortical tumour."

The evidence reported by Holmes [14], which has been mentioned above, is entirely in favour of the theory of localization that has been adopted in my first cerebellar study in 1918.

Here follows a description of my own two clinical observations, which seem to support the idea that the cerebellar centres in man are arranged in a manner analogous to that found in mammals.

Case 1.—K. G. B., janitor, aged 51 years. Clinical diagnosis : tumour of biventral lobule of the cerebellum ; metastasis from a rectal carcinoma.

Admitted to the medical clinic on August 24, 1918 ; died September 29, 1918. The patient enjoyed good health until the beginning of 1918, when trouble with defæcation, tenesmus and diarrhœa appeared. He remained at work until the end of July, but had lost about 25 kg. during the year. In August he developed severe headache, referred to the neck, and vomiting.

The patient was received into the Lund University surgical clinic (Professor Borelius) on August 15. In this clinic a rectal cancer was found which could not be operated upon owing to its high position in the pelvis. Ophthalmoscopy on August 12 (Dr. Franck) showed the fundus normal. The persistent severe headache and vomiting made a metastasis in the central nervous system very probable, and the patient was therefore referred to the medical clinic for a neurological examination.

Abstract from the records in the medical clinic : The patient complains of severe headache, especially in the region of the neck. He is somewhat dull and slow, but answers correctly. On moving in bed he has paroxysms of vomiting and vertigo, especially on turning his eyes towards the right. He usually lies motionless in the bed, with his head turned to the right.

The right plantar reflex was extensor (Babinski), the left flexor, but no other abnormal signs were found except these referable to disturbance of the functions of the cerebellum. It must be especially emphasized that there was no sign of paresis in the right leg. The Achilles and patellar tendon reflexes were normal on both sides. No clonus was present. Romberg's sign was positive, but there was no tendency to fall in any constant direction. There was horizontal nystagmus, with its rapid phase towards the right, and slight adiadokokinesis in the pronation-supination test in the right arm, but none in left. The finger-nose test is carried out promptly on both sides. The knee-heel test is accurate on the left side but much disturbed on the right, the patient throws the right heel roughly and clumsily beyond the left patella up to about the middle of the left thigh, and in moving the right foot back to a spot marked by the examiner's finger on the lower part of the left leg the spot is also passed, though not so far. With the right leg this test is always repeated with the same inaccuracy. This is the more remarkable as the finger-nose tests with both arms, and the knee-heel test with the left leg, are performed with normal precision.

No spontaneous past-pointing from the shoulder-joints either in the vertical or horizontal plane. He also points correctly with the left leg from the hip-joint, but when lying on his back there is considerable past-pointing inwards (medialwards) with the right leg.

Syringing the right ear with cold water produces nystagmus towards the left and past-pointing to the right of both arms from the shoulder-joints, and of the left leg. The right leg deviates towards the left. No tendency to falling is evoked. Syringing of the left ear produces reinforcement of the nystagmus towards the right, past-pointing of the left arm towards the left, and of the right arm to the right, past-pointing in the left leg, wide deviation of the right leg towards the left, and falling towards the left.

Intense vomiting occurred after syringing.

August 27.—To-day the patient falls spontaneously backwards and to the right. Only slight adiadokokinesis in the right arm, none in the left. Finger-nose test prompt and accurate on both sides. The knee-heel test is performed with the same apparent excess of motor innervation as before, the right foot being thrown far above the left knee. With the left foot the movement is performed normally. No paresis of the musculature in the right leg. When told to raise himself from supine into the sitting position with the arms crossed on the chest he fails to sit up because the feet, and especially the right leg, rise from the bed. When in the standing position he attempts to put the point of the foot upon spots marked by chalk on the floor, the right foot is always moved in a clumsy way far past the mark, even when the patient controls the movement with his eyes. This is more striking when he has to move the foot backwards. Spontaneous pointing unchanged; after rotation to the right on a chair (ten turns in twenty seconds according to Bárány's method) a strong tendency to fall towards the right, with past-pointing to the right in both arms and in the left leg (hip-joint), but none in the right leg. After rotation to the left, past-pointing in both legs and in the left arm, but none in the right arm. After rotation with his head flexed toward the right or left shoulder alternately, the patient can be made to fall backwards or forwards.

During the first week in the medical ward the functions of the cerebellum were examined daily. He was, however, very much troubled by examination and began to vomit intensely as soon as he had to change his position or move himself in any way. Moveover, he suffered much with headache, and during the first week became dull. This of course had an unfavourable effect on the results of the examinations, especially on the testing of the vestibular functions (caloric and rotation tests), but it was possible to carry out without discomfort to him the tests for adiadokokinesis, and the finger-nose and knee-heel tests. Spontaneous pointing from both shoulder-joints remained normal; there was only a slight adiadokokinesis in the right arm; the finger-nose test was performed promptly with both arms, and the knee-heel test with the left. There was a constant deviation inwards of the right leg in pointing while he lay supine, and the spontaneous movements of this extremity were always irregular and clumsy, especially in the knee-heel test. These disturbances were considered to be of cerebellar origin. The general condition of the patient became gradually worse; the somnolence and dullness increased gradually and he died on September 29.

Owing to the cerebral symptoms a cranial tumour was suspected, probably a metastasis from the rectal neoplasm. Since the clinical disturbances were mainly of cerebellar nature this tumour was localized in the cerebellum, and as the symptoms affected the right leg only the tumour was placed in the leg centre of the right cerebellar hemisphere. The existence of a leg-centre in the human cerebellum has never been demonstrated, but from analogy with the mammalian cerebellum I assumed that it lay in the lobulus biventer.

The autopsy made by Dr. J. Fex completely verified the diagnosis. In the right biventral lobe a tumour was found, which on the microscopical examination turned out to be a metastasis of the rectal cancer. (Figs. 3A and 3B).

The cerebrum was free from pathological changes. The cerebellum was normal in shape, but the right hemisphere was somewhat more voluminous than the left. The architecture of the fissures and lamellæ was everywhere normal, except in the biventral lobe on the inferior surface of the right hemisphere, where the tissue was firmer to the palpating finger. Over a certain area the cerebellar surface was replaced by a greyish-looking firm mass around which the lamellæ curved as if they were pressed apart. In frontal sections it was seen that this was part of the tumour. Its greatest horizontal diameter was 5 cm. and vertical 4 cm. It lay entirely within the lobulus biventer, if the lobulus gracilis is considered apart from this. It occupied the whole medial mass of this lobule on the inferior surface of the hemisphere, and was only covered by a thin layer of cortex until the fossa transversa (Ziehen) and flocculus were reached. It was sharply limited by the deep fissure that separates the lobulus gracilis from the lobulus biventer, and spread from here laterally and backwards in the substance of lobulus biventer to the region where the lower anterior surface of the hemisphere borders on the lower posterior surface.

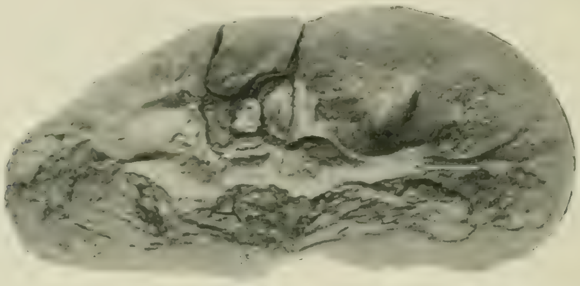

FIG. 3A.—Transverse section through the cerebellum of Case 1. The tumour is seen in its subcortical position on the right side. The white substance and the nucleus dentatus are compressed but otherwise undamaged.

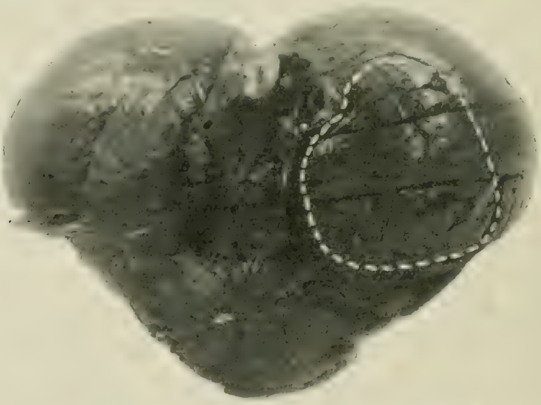

FIG. 3B.—Cerebellum of Case 1. The area surrounded by the white broken line indicates the site and size of the tumour.

The lower peripheral branches only of the central white substance were involved by the tumour; the main mass was free, but was displaced upwards and backwards. The dentate nucleus also escaped, but its central foldings were pressed somewhat dorsally, and its hilus was compressed.

No other tumours were detected in the cerebellum. The medulla oblongata was a little dislocated towards the left side in the vicinity of the tumour, and was somewhat compressed on its right side. Microscopical examination of the tumour showed it to be a soft carcinoma with a tendency to central necrosis.

The fact that the Babinski sign was positive on the right side is naturally explained by the pressure exerted by the tumour on the pyramidal tract. The section clearly revealed that such a pressure had occurred. The absence of all other signs of a pyramidal lesion makes it impossible to ascribe the motor disturbances of the right leg to the slight impairment of the pyramidal tract, of which the right extensor response was an indication.

Summary.—In this case of cerebellar tumour the clinical symptoms were limited to the right leg, apart from slight adiadokokinesis in the right arm. At the autopsy a tumour was found in the right lobulus biventer of the cerebellum.

There are many arguments, anatomical and others, which strongly support the view that this lobe is related to the functions of the leg. This is the first described human case that in a clear and convincing way shows that the leg-centre is situated in the posterior part of the cerebellar hemisphere, in a position homologous to that which it occupies in the mammalian cerebellum. The site of the tumour was an extremely favourable one, since it occupied the entire posterior region of the lobus posterior (mihi) and this region only.

Case II.—E. M., girl, aged 16 years. Clinical diagnosis: Cerebellar tumour. Pathological diagnosis: Sarcoma of the meninges with extensive growth over the surface of the brain and spinal cord.

The patient's illness began with severe headache and vomiting in the beginning of 1921. After some months a staggering gait developed. In consequence of the severe headache, which was mostly localized in the neck, the patient was received into the University Clinic for Internal Medicine on September 21, 1921. She then had nystagmus, mainly horizontal, of a vestibular type; the right pupil was smaller than the left, and flexion of the head forwards was painful, but flexion backwards not so. Romberg's sign was positive. Gait, even with the eyes open, was very uncertain; she staggered equally to the right and left. The finger-finger, finger-nose and knee-heel tests were performed accurately on both sides. There was no adiadokokinesis. In the right arm there was spontaneous lateral past-pointing from the shoulder-joint, but no error in the left arm. Ophthalmoscopical examination

(Professor Ahlström) revealed choked discs with a swelling of more than seven diopters in both eyes. Vision was seriously impaired.

November 1: Otological examination (Docent Törne): Drums of both ears normal. Hears whispering with both ears at 4 metres. Spontaneous horizontal nystagmus to both sides. Reactions to the caloric test (cold water) perfectly normal on both sides.

November 8: Constant spontaneous past-pointing towards the right with the right arm. Tendency to fall to the right.

November 11: Finger-nose test normal. Romberg's sign negative. Gait normal with the eyes open, but when they are closed the patient deviates towards the right in walking.

November 12: The nystagmus disappears when she turns the eyes to either side for a time. She performs rapid alternate movements well, but somewhat better with the left hand than with the right.

In consequence of the disturbed vision the patient was referred to the surgical clinic, where a trepanation was performed by Professor Gustaf Petrén on November 14.

Abstract from the record of operation.—After opening the posterior fossa on the right side and incising the dura, the cerebellum was found to be under high pressure. Some suspicious looking substance was removed with a sharp spoon from the lateral part of the opening. Punctures were made in two spots of the cerebellar hemisphere to a depth of 3 to 4 cm., but nothing was found, and no tumour was palpable to the finger. As the cerebellum was pressed out of the opening its margins were lacerated. The skin-flap was replaced and the wound sutured; considerable pressure was thereby exerted on the protruding cerebellar hemisphere. The patient was in good condition after the operation.

A microscopical examination of the tissue excised was made at the Pathological Institute by Professor Sjövall: "No signs of tumour or tuberculosis, but in certain regions of the mass there were hæmorrhages, some of long standing. These indicate with certainty an underlying process with secondary toxic or circulatory disturbances in the surrounding substance."

For some time after the operation the patient had intense cerebellar ataxia with typical cerebellar speech. The right eye was deviated to the right, but the other movements of the eyes were normal. There was marked nystagmus to both sides. The right facial nerve was paretic. She heard whispering with each ear at three metres. No paresis of extremities or trunk, and sensibility was everywhere normal. Movements of the right arm were very irregular, slinging and unbalanced. In the finger-nose test the right hand was thrown with force past the nose, or against the forehead, but in this test the left arm was normal. The inferior extremities also showed the same disturbance in movement, the knee-heel test being badly performed on both sides, especially on the right. The patient was unable to sit up in bed without shaking.

This severe general ataxia was the most prominent feature after the operation. After being treated with Röntgen-rays she was then sent home on

February 19. Her condition had at this time slowly improved, so that she could walk, but her gait had the characteristics of cerebellar ataxia.

While at home the patient improved considerably, she had only moderate headache, and no vomiting or vertigo. Her vision improved too. She was able to walk alone and said she did not stagger. She was received into the hospital again on March 3 in order to continue the X-ray treatment.

On her arrival she had a hernia the size of an orange at the site of the trepanation. She is intelligent and bright. She could count fingers at one to one and a half metres with either eye, but her discs were atrophic. There was marked nystagmus, especially in looking to the right. There was no paresis, and the plantar reflexes were normal.

The finger-nose test with the right arm was uncertain, the hand developing a slight tremor at its goal. There was also adiadokokinesis of the right arm and in the left to a less extent. The knee-heel tests were normal on both sides. Romberg's sign was not present but gait with open eyes was staggering and uncertain, the patient sometimes tumbling to the right. Both arms deviated to the right in the past-pointing test in the horizontal plane, but there was no deviation in the vertical plane.

April 4.—Syringing the right ear with cold water produced brisk nystagmus when the eyes were turned to the left, none when they were turned to the right; exaggeration of the past-pointing to the right, and the patient fell to the right. On turning the head to the right the patient fell backwards, on turning it to the left, forwards.

April 8.—Marked nystagmus to the right, none to the left. The finger-nose test shows typical ataxia of the right hand, none in the left.

The patient was again sent home on April 21, after she had three further applications of X-rays. She remained at home till May 18 when she was again admitted to hospital. She had had some headache while at home. Her gait was normal, though she sometimes tumbled to the right; she had fallen only once, when she tried to run. She had nystagmus on turning her eyes to either side, more marked to the right. Sensibility was everywhere normal, and no paresis was detected. Romberg's sign was absent. The finger-nose test showed a slight uncertainty in the right hand, but none in the left, and there was marked adiadokokinesis in the right arm. The knee-heel test was carried out promptly, but there was a slight uncertainty in the movements of the right leg. Gait was staggering and uncertain, and became only slightly more so when the patient closed her eyes.

May 29.—No past-pointing with the left arm, but the right deviated towards the right.

May 30.—The finger-nose test was normal with the left arm, and only slight disturbances in the last phase of the movement in the right. There was marked adiadokokinesis in the right arm, and slighter in the left. On closing her eyes when her feet were together the patient stumbled but did not fall. She walked with her feet widely separated and stumbled slightly.

June 2.—Gait almost normal.

The patient left the hospital on June 22. She was admitted again on August 28 with severe headaches and a large hernia at the site of the operation. She was unable to turn her eyes to the right, and had paresis of the right facial nerve. There was adiadokokinesis on both sides, especially on the right. The finger-nose test was carried out poorly with the right arm, the finger hitting the nose or its vicinity with great force. The knee-heel test was also uncertain on the right side. The arms deviated in various directions in testing for past-pointing owing to the disturbances of movement.

The patient later developed a slight hemiparesis on the right side of the body, became unable to stand or walk, and died on October 2.

An autopsy was performed October 2, 1922 (Professor Sjövall, Dr. Olinder).

A meningeal tumour was found in the right side of the posterior fossa; it also spread widely over the meninges of cerebrum, cerebellum and the spinal cord. It formed a thick layer around the spinal cord throughout its whole length.

The cerebellum, after fixation in formol, was carefully cut in frontal sections. It was then found that the entire left hemisphere was normal and that the vermis had retained its structure, although infiltrated by the tumour, especially in the uvula and nodulus. This infiltration increased on the right side of the vermis, but the right tonsil and a small part of the digastric lobe in the neighbourhood of the tonsil, corresponding to its medial and lower anterior parts, were comparatively well preserved. No trace of cerebellar structure could be recognized in the rest of the digastric lobe. The semilunar lobes had disappeared and the destruction extended into the right part of the lobulus simplex and into the posterior part of the right side of the lobus anterior.

There was a softening of the central white substance below the cortical destruction. No trace of the dentate nucleus could be seen and no normal tissue was found above the level of the peduncles. The nuclei tecti were intact.

Microscopical examination showed that the growth was a meningeal sarcoma.

Summary.—The patient was a girl who, owing to signs of increased intracranial pressure (choked discs with impaired vision), was trephined over the right cerebellar hemisphere, and part of the lateral portion of the cerebellum was removed. After the operation she developed a severe generalized ataxia, undoubtedly due to the intense pressure and tension on the whole cerebellum. The ataxia diminished gradually, and undoubtedly as a consequence of X-ray treatment the general condition of the patient improved in a remarkable way. For a long period she presented no other neurological symptom than signs of cerebellar disturbances in the right arm. Her gait was almost normal, Romberg's sign was absent and the knee-heel test was well performed with the right leg; but there was ataxia in the finger-nose test and adiadokokinesis of the right arm. Towards the end of her life the most prominent feature was again a general ataxia of the whole body, and hemiparesis. This was undoubtedly caused by the tumour masses found at the autopsy.

The period of temporary recovery was that of greatest interest in this case. We know that such tumours can be influenced by X-rays, and we may therefore assume a regression of the tumour mass leading to the regression of the symptoms. That being so, it is remarkable that during the whole time there was a profound ataxia of the right arm.

A portion of the lateral part of the anterior semilunar lobe had been removed at the operation, and the cortex round the margins of the opening of the skull was lacerated. Later the skin-flap compressed the protruding hemisphere. From earlier cases treated in the same way and studied especially with regard to disturbances of speech, I know that such an operation means a considerable destruction of the cerebellar substance that protrudes into the opening. Undoubtedly the entire cortex of this part of the cerebellum must have been destroyed, directly or indirectly, by the operation. The autopsy verified this assumption.

The anatomical examination in fact showed that both semilunar lobes, the lobulus gracilis, and the rostral parts of lobulus biventer were destroyed. The extensive softening of the central white matter of the right hemisphere is here left out of account, because it had all the characteristics of an acute process which occurred shortly before death. The symptoms exhibited by the patient during her last few weeks have no interest for the questions discussed in this paper.

For a time after the operation there was an intense general cerebellar ataxia in both sides of the body. This may be regarded as an ordinary result of such operations on the posterior fossa. This ataxia diminished gradually, but for several months there was ataxia of the right arm, whereas the cerebellar disturbances of the right leg were only slight. The discrepancy between the symptoms of cerebellar deficiency in the arm and the leg is the most interesting feature of this case. How is it to be explained? According to the theories developed above, the centre of the arm is located in the upper semilunar lobe, whereas the leg-centre is situated in the lobulus biventer and the tonsil. In this case the semilunar lobes were entirely removed, and the remaining parts of the biventral lobe and the tonsil were sufficient to regulate the motor functions of the leg.

Thus the symptoms of this case also are in favour of the hypothesis that the arm-centre of the human cerebellum is situated rostrally to the leg centre. This case, therefore, forms a natural complement to the first case described.

Bárány [3] has studied the clinical symptoms of vestibular lesions in an ingenious manner, and has been led by this work to a conception of another system of cerebellar localization. According to him the vestibular reactions (past-pointing, tendency to fall) produced by irritation of the vestibular apparatus, are elicited by way of the cerebellar cortex. The works of the Dutch physiologists, Magnus and de Kleijn, however, disprove this hypothesis upon which his whole system of localization is based. They have found that the ordinary reactions of the extremities and trunk evoked by irritation of the vestibular apparatus are not in any way influenced by total ablation of the cerebellum. They have thus conclusively shown that the reflex mechanism of the vestibular reactions is not related to the cerebellum.

On the other hand, Bárány has conclusively shown that reactions similar to those appearing after vestibular lesions may be elicited from the cerebellum. Thus he has found that after cortical lesions of the cerebellum typical deviations of the limbs occur (past-pointing in different directions). Bárány's results have been corroborated by several authors, as Holmgren, Berggren, Boivie, Schmiegelow and others. Trendelenburg's method of cooling the cerebellar cortex has proved to be a useful mode of investigation. By cooling different areas of the cerebellar cortex Bárány has been able to produce deviations in different directions in the past-pointing tests.

Bárány believes that the main principles of cerebellar localization is a representation of the different directions of movement at the joints. As each joint can be moved in four directions, upwards and downwards, medially and laterally, it must be represented in the cerebellar cortex by four tonus centres, one for each direction of movement. If one centre is paralysed by a lesion or by cooling, the antagonistic centre prevails, and the result is a deviation in the direction of the action of this antagonistic centre. Thus, if the inward centre for the arm is disturbed, the arm deviates laterally in the pointing test. Bárány has lately reviewed this theory [3].

The situation of the tonus centre for inward deviation of the arm seems to be well established ; paralysis of it produces past-pointing of the arm. This can be easily induced by cooling the cerebellar cortex with ethyl chloride in persons in whom the mastoid process has been removed, so that the dura lies directly under the skin ; this produces deviation outwards of the homolateral arm. Bárány says that he has been able to perform this experiment at least forty times with the same result, and he therefore considers this centre is definitely established..

Gordon Holmes, who has made an extensive study of injuries of the cerebellum during the war [13], concludes his studies of the pointing reaction by stating that in almost all his cases there was a tendency to past-pointing outwards, wherever the lesion was situated in the cortex. This is a strong objection to the supposition of a special tonus centre for inward deviation.

The present writer [21] has recently found that past-pointing can be induced from a purely spinal mechanism. If a person stands with his feet close together and points towards a given point, his finger will deviate laterally if during the test the other arm is abducted. This lateral past-pointing depends only on the disturbance of the static conditions of the body produced by the abduction of the other arm. I have called this phenomenon *spinal past-pointing.*

Thus a disturbance of the static conditions of the body gives rise to past-pointing. From experimental investigations we know that a lesion of the cerebellum produces disturbances of muscular tone, that is, static disturbance of different parts of the body, and it seems to me that the only one of Bárány's observations that has been definitely established, namely, the past-pointing outwards, may be explained as a secondary phenomenon produced by a general disturbance of static conditions following any lesion of the cerebellum.

Bárány has described a tonus centre for downward deviation in the medial part of lobulus semilunaris inferior, close to the vermis. Destruction of this centre should give rise to past-pointing upwards of the arm. One of my patients in whom there was a solitary tubercle situated exactly in this region, nevertheless pointed downwards before the operation [18]. The tumour was successfully removed by Professor Borelius. On the excised piece of the cerebellar cortex it was easy to recognize that the tissue removed was the medial part of lobulus semilunaris inferior. After the operation there was no deviation. This, which must in all respects be considered a pure case, strongly contradicts Bárány's hypothesis of a tonus centre for downward deviation in this region ; Bárány himself [3] admits that it is a serious objection to his hypothesis.

According to Bárány the centre of the leg and arm are situated together in lobulus biventer. He denies that the arm and the leg are represented in a manner analogous to that determined by experiments on animals. That past-pointing is produced from the same region of the cerebellum in either the leg or in the arm can be, it seems to me, explained by the fact that any lesion of the cerebellum brings about a disturbance of static conditions of the body, and that this results in past-pointing of different parts of the body.

Conclusions.

The basal portions of the cerebellum, situated immediately above the fourth ventricle, are phylogenetically the oldest parts of the cerebellar cortex. Special attention must in future studies be paid to these parts, which have hitherto been neglected. Anatomical facts indicate that they are endowed with important functions.

The most characteristic feature of these basal regions is that they receive fibres directly from the vestibular nerves, according to studies previously made by the author.

The histological uniformity of the cerebellar cortex, even in the human cerebellum, indicates that function and organization of function are probably essentially the same in the whole organ. All evidence on the function of the basal regions will therefore be of the greatest value for an understanding of that of the whole cerebellum.

After lesions of the basal parts motor phenomena known as "forced movements" occur.

It has been shown by Russell, Ingvar, and Simonelli that these forced movements after lesions of the posterior lobe appear chiefly as a falling backwards. These same authors have demonstrated that the more posteriorly the lesion lies, the more pronounced is this falling backwards during the acute stage.

Since the forced movements resemble strongly those appearing after lesions of the vestibular apparatus, it is logical to regard the forced movements after cerebellar lesions as being due to disturbance of the vestibular innervation of these parts.

Both the vestibular and cerebellar forced movements always take place in a definite plane of space. When such lesions involve the anterior or posterior parts of the basal region the forced movements take place in a sagittal plane around a frontal axis, while lesions of the lateral parts of the cerebellum give rise to forced movements in the frontal plane around a longitudinal axis.

Since those associated with lesions of the anterior and posterior parts of the vermis resemble those produced by lesions of the vertical semicircular canal, it is logical to conclude that this canal is specially connected with these regions of the cerebellum. Certain clinical observations speak in favour of this hypothesis.

The fact that forced movements disappear soon after the infliction of the lesion is not an argument that they are not of cerebellar origin, or without importance for our knowledge of cerebellar physiology.

As the basal regions of the cerebellar cortex with their intimate vestibular connections are, in the literal sense of the word, a sort of calyx which encloses the major part of the cerebellum, which is developed later in phylogenesis, so the functions of the labyrinth may be considered to include in embryo those of the cerebellum. There is during phylogenetic development a tendency of regression of the vestibular influence on cerebellum, whereas the spinal influence increases (strongly developed spino-cerebellar tracts in higher animals). Morphological and histological studies have provided ample evidence that the cerebellum is an identical organ in all vertebrates. There exists a complete homology between all parts of all cerebellums, except in the case of the bony fishes. Accordingly, in all the same system of functional localization must hold.

A long series of experiments on the cerebellum has shown that in animals the limbs are at least to a considerable extent represented in special regions of the cerebellar cortex (lobulus ansoparamedianus, Bolk), and that the centre of the fore limb is situated rostrally to that of the hind limb.

Two cases are described in this article which strongly support the view that in the human cerebellum there is the same arrangement of the centres of homologous parts.

In the first case, where a tumour lay in the right lobulus biventer, the only clinical symptom was cerebellar ataxia of the right leg. In the second case the right hemisphere was injured extensively by an operation, and post-mortem examination showed that a large part of the hemisphere (semilunar lobes, lobulus gracilis, part of lobus biventer) had been completely destroyed. The severe general ataxia that followed the operation disappeared gradually from all parts of the body except in the right arm, though a slight disturbance of a cerebellar type was also noticed in the right leg.

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THE OCCURRENCE IN OSTEITIS DEFORMANS OF LESIONS OF THE CENTRAL NERVOUS SYSTEM, WITH A REPORT OF FOUR CASES.

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MUCH has been written on osteitis deformans since Paget first gave his classic description of this disease in 1876. It is well known that the nervous system is rarely affected, in spite of the alterations that occur in the bones which surround the brain and spinal cord, as well as in the neural foramina of the skull and vertebral column. The rarity of cases reported in the literature in which neurological signs were present is striking.

The essential changes of the disease consist in a primary absorption and rarefaction of bone, followed by an excessive formation of fibro-osteoid tissue. In this way the consistency of the affected bones becomes softened. These lesions occur most frequently in the bones of the skull, the long bones of the extremities, and very often in the vertebral column.

In the cranium extensive alterations are produced by the abnormal condition of the bones. While the facial bones are not infrequently affected, attention here is chiefly concerned with the osseous structures which envelop the brain. The skull is increased in size. In shape it commonly becomes more square and may show bossing. The latter deformity is seen most frequently upon the vertex. An increase in width is an outstanding feature of the altered shape of the head. In many cases the sides of the skull bulge prominently, so that the ears come to be tilted outwards. Prominence of the frontal region is also frequently present.

The cranial bones are increased in thickness, often to an extreme degree, and the sutures, especially at the vertex, are frequently obliterated. Differentiation into outer, middle and inner tables of a severely affected bone, seen in section, is seldom possible. On the inner aspect of the cranial vault the greatest thickening and irregularity are commonly seen in the region of the frontal and anterior halves of the parietal bones. In this area flattened exostoses are sometimes present, producing great unevenness of the bony surface. The occipital bone, though participating in the general increase in thickness, usually has a less irregular surface. The bones at the base likewise become thickened.

The sella turcica in a few cases has been found altered in shape, the alteration consisting in a flattening out of the fossa, but in a series of six skulls Hurwitz found the sella turcica altered in one only. Léri and Jefferson both mention cases in which the fossa had become very shallow. In Jefferson's case, which was examined radiographically, the sphenoidal sinus appeared very large. On the other hand this sinus may be greatly reduced in size; I have recently had the opportunity of examining a skull, severely affected by osteitis deformans, in which it was filled in by bony overgrowth.

The internal configuration of the skull is markedly altered. As mentioned before, an increase in its breadth is an almost constant feature. This widening is not only accounted for by the greater thickness of the bones, but also by an actual increase in the transverse diameter of the interior. The antero-posterior diameter is lengthened, but to a less extent. The vertical measurements of the cavity, however, are decreased, especially in the region of the foramen magnum, as has been pointed out by Léri.

That portion of the base surrounding the foramen magnum which is supported by the spinal column is maintained in position, while the various cranial fossæ tend to sag down around this central point. An important factor in the production of this sagging is the weight of the cerebral hemispheres. The peripheral portions of the lesser wings of the sphenoid and of the petrous temporal bones sink downwards. At the same time the degree of upward slope of the anterior or basilar portion of the occipital bone and of the dorsum sellæ becomes reduced or lowered. In this manner the base of the skull comes to be flattened out to a certain extent. This altered formation has been termed "platybasie" by Léri.

In more extreme cases of sinking of the peripheral portions of the base, the basilar part of the occipital and posterior part of the sphenoid bones may actually have the appearance of having been pushed up into the cranial cavity, producing an elevation. To this deformity Léri gives the name of "convexobasie."

It has long been recognized that the neural and vascular foramina at the base become reduced in size, though some observers have made a contrary statement. Léri, however, in 1913 drew particular attention to the narrowing of all the basal foramina, including the foramen magnum, in skulls affected by osteitis deformans.

The extent of reduction in the calibre of the individual foramina is commonly unequal, depending upon the degree of abnormality in the bones surrounding them. While the reduction in size of the neural foramina may be accepted as a constant feature, narrowing of the vascular foramina is by no means always present. In the first case described by Paget enlargement of all the channels and apertures for blood-vessels was noted at the autopsy. Humphry reported in one case increase in size of the carotid canal and of the foramina spinosa. It is usually observed that the grooves on the inner surfaces of the bones for the meningeal vessels are much deeper than normal. The pulsatile properties of the vessels may have something to do with this.

The absence of cerebral compression in osteitis deformans of the skull has been accounted for by the intracranial pressure exerting its influence upon the bones in their softened condition, at the time the cranial deformities develop. Consequently, though the various diameters of the cranial cavity may be altered, the capacity of the skull in osteitis deformans has not been found to differ from that of the normal.

On the other hand the freedom from compression of the cranial nerves in almost all cases is more difficult to understand. Two cases will be described later in which, however, both the optic and ocular nerves were involved (Cases 3 and 4).

Osteitis deformans of the vertebræ commonly gives rise to static deformities, such as curvature, rigidity and diminished stature. Hurwitz reports cases in which gradually as much as 7¼ to 13¾ inches have been lost in height. While in the majority of patients these changes are due to the softened condition of the bones, in some a shrinkage of the fibrous and cartilaginous attachments of the vertebræ has appeared to be the only cause present.

The curvature is usually rounded and very seldom angular. Deviations of a scoliotic nature are relatively infrequent. Cases have been reported in which the spine was straight and yet the vertebræ were extensively affected.

While most of the vertebræ are usually affected to some degree in osteitis deformans of the spine, it is not uncommon to find crushing and obvious deformity limited to a few contiguous vertebræ. Or the body of one vertebra may be much reduced in depth and sometimes displaced.

Lipping of the lateral edges of the bodies is a common deformity; these exostoses sometimes unite over the intervertebral discs. Such bony hyperplasia is often extreme and may produce an appearance as if candle grease had trickled down the sides of the vertebræ. The spinous processes are usually held firmly together by an osteo-fibrotic ankylosis. The intervertebral foramina in those areas of the spine most markedly affected are often considerably reduced in size in an irregular manner; it is, therefore, the more remarkable that radiating pains, such as could be attributed to compression of the dorsal roots, are infrequent.

The possible deformities produced by osteitis deformans of the vertebræ, as they affect the lumen of the spinal canal, have been practically disregarded in the literature of the disease. That the canal may be reduced in size even to the extent of compressing the spinal cord, will be made clear by the descriptions of two of the cases which follow. This complication must be rare, as no reports on similar cases have come to my notice in the literature. I have also been able to prove that reduction of the calibre of the spinal canal and irregularities in its walls may develop in osteitis deformans by the examination of the vertebral column of a cadaver.

The two cases of compression of the spinal cord which occurred in patients suffering from osteitis deformans were admitted to the National Hospital, Queen Square, one under the care of Dr. Gordon Holmes, the other under Dr. Kinnier Wilson, to whom I am indebted for permission to make the following reports.

Case 1.—J. H., aged 55, clerk, was admitted November, 1922. He gave no history of injury. He had been operated upon for rectal fistula when aged 45. He had contracted gonorrhœa twice in youth; his health otherwise had been excellent, and he had led an active life. Both his parents were healthy; he was the only surviving child, one other infant having been born dead. He himself had four healthy children, while two others died in infancy.

In September, 1921, he began to experience a sharp lancinating pain in the buttocks when walking. He also noticed that his feet always felt cold, although previously he had been troubled with hot feet. Shortly afterwards he noticed that the right leg was becoming weak, and later the left leg began to feel stiff. He found he could walk one mile only without the aid of a stick.

Towards the end of 1922 both legs became much weaker, but he could still "shuffle" along with the aid of two sticks. On attempting to walk he had pain like sciatica down the left leg. Six months previous to admission he had noticed, while having a hot bath, that the water felt cold to his feet.

Bladder trouble, in the form of straining and frequency of micturition, had been present for four months. The bowels were constipated and rectal control was defective after purges. For six weeks before admission he had "muscle spasms" commencing at the knees and spreading up as a tight feeling to the middle of the abdomen. There was no definite girdle sensation. The spine in the lumbar region was tender.

On admission patient was of a stout, plethoric build with a high complexion. His weight was 13 st. 6 lb. The features betrayed no deformity of the facial bones. The skull was large and prominent, and bulged over both ears, with a high boss over the forehead. He stated that "a hollow across the top of the forehead had become replaced by a lump." Two to three years previously he wore size $6\frac{7}{8}$ in hats, but now required $7\frac{1}{2}$ size. The top of his head sometimes ached and felt hot. Only the front lower teeth remained; these were in proper alignment, and did not show signs of "alveolite expulsive," a condition described by Léri in which owing to the maxillæ being affected the dental alveoli became reduced in size and the teeth slowly expelled. His neck was short and thick and his head inclined slightly forwards. In the lower cervical and upper dorsal region the curve of the spine was more rounded than normal. When standing the patient showed a distinct stoop, and had difficulty in raising the head to look upwards. He remarked he was not as tall as he formerly was. The left tibia in its lower third presented a hard and painless fusiform swelling. On passive manipulation there was no limitation of movement at the ankle-joint. There was no external evidence of deformity, other than in those parts of the skeleton already mentioned.

The ocular fundi were normal, no lens opacities were discovered and the visual acuity was unimpaired. The functions of the cranial nerves were unaffected.

No motor or sensory disturbance was present in the upper extremities. On the trunk, below the level of the third costal cartilages and including the lower extremities, there was an impairment of moderate degree to all forms of sensation, and immediately above the upper level of this sensory disturbance a narrow zone of hyperæsthesia. The action of the intercostal and abdominal muscles was poor. Both legs were paretic, the right being weaker than the left. No muscular wasting was observed.

The superficial abdominal reflexes were absent. The plantar responses were extensor in type. The deep reflexes of the lower limbs were exaggerated.

In the cardio-vascular system the radial arteries were moderately thickened and the pulse tension raised. The temporal vessels were tortuous. The cardiac dullness was increased on the left to beyond the nipple line. In the examination of the other systems no abnormality was detected.

Lumbar puncture was unsuccessful. Considerable difficulty was met with in entering the spinal canal, as the needle everywhere encountered bone, the consistency of which was softer than that of the normal. Finally, when the point of the needle penetrated the theca no fluid escaped. The Wassermann reaction of the blood was negative.

On radiographic examination the bones at the vertex of the skull showed marked thickening and mottling. The outline of the outer table was faint and very hazy in the fronto-parietal region. That of the inner table was more dense but definitely irregular in the same area. The outlines of the occipital bone were smooth but showed a sinking of the occipital fossa in relation to the foramen magnum. At the base the bones gave the appearance of a flattened surface similar to the type of "platybasie" of Léri. In the region of the mastoids the air cells appeared enlarged and the bone rarefied. The sella turcica was unaltered in size, but the sphenoidal sinus appeared larger than normal. The palatal bone appeared to have been tilted slightly downwards and forwards.

A skiagram of the upper dorsal spine indicated the presence of lipping of the edges of the vertebræ. The lower half of the left tibia showed signs of rarefaction with increased thickness of the outer compact layers, especially on their mesial aspect; the bone was bowed forwards, thus increasing the space between the tibia and the fibula.

In this case, because of the slowly progressive character of the patient's disability and the evidence of localized compression of the spinal cord, operative interference was decided upon. On November 28, 1922, Mr. Percy Sargent performed a laminectomy of the second to the fourth dorsal vertebral arches. At the operation the bone was found thickened and softened, cutting easily with the forceps. The perithecal space was absent and the inner surfaces of the laminæ lay in close apposition to the dura mater. Pulsation of the dura was at first very feeble, but improved as the decompression was effected.

A good recovery was made by the patient, and two months later he was discharged able to walk with considerably greater ease than on admission. The sensory disturbances were unchanged in the level to which they had previously attained, but were greatly diminished in degree. Sphincter control was almost completely regained.

A piece of bone removed at operation showed microscopical changes typical of osteitis deformans. Rarefaction was observed and osteoclasts were numerous, in many cases lying against and eroding the bony lamellæ. The latter were very irregular in direction and in places outlined by a row of osteoblasts. A highly cellular fibro-myxomatous looking substance occupied the spaces between the lamellæ.

Case 2.—V. C., aged 63, was admitted March, 1920. His previous health and family history revealed no points of importance. No history of venereal disease was obtained.

When 49 years of age he began to suffer with sciatica of both legs. The neuritic pains were associated with spasms and cramps in both legs, and he had some difficulty in controlling his urine. These symptoms disappeared within a period of two years.

At the age of 61 he underwent an operation for the removal of hæmorrhoids. A short time previous to the operation he had observed that his feet often became numb and blue. Soon after the operation he noticed that his legs were becoming unsteady, and he fell down on several occasions.

Within the space of a year he began to have difficulty in raising his feet off the ground, and the legs felt heavy. He also began to experience a sensation like that of a tight band round the upper part of the abdomen. It was only on being medically examined that he discovered that he had lost sensation in his legs. Subjectively there was some numbness in the feet only. He did not have any pain in the limbs and the spine was not tender. The paralysis of the lower extremities rapidly became complete. Bladder trouble was present in the form of precipitant micturition, and rectal control was defective.

On admission to hospital he was thin, but looked younger than his age. The vertebral column was very rigid and showed a prominence of the ninth dorsal spinous process, but no angulation. The spinal curves were not exaggerated. No other skeletal deformities were noticeable. He usually lay in bed with the legs drawn up and flexed at the knees. The arterial system showed marked tortuosity of the superficial arteries and the vessel walls were thickened.

The cranial nerves were unaffected, the fundi were normal and no signs of cataract were present. Sensory disturbance over the trunk and lower limbs was evidenced by an almost complete loss to tactile, painful and thermal stimuli up to the level of the xiphoid cartilage. The appreciation of vibration was absent below the level of the seventh dorsal spine. In the lower limbs there was a complete loss of the sense of position in space.

Paralysis in flexion was present in the legs. The lower intercostal muscles did not act, and breathing was mainly diaphragmatic. Changes in the tendon reflexes consisted of exaggeration of the ankle-jerks. The knee-jerks, however, were difficult to obtain, owing to the degree of spasticity present. The plantars were extensor in type, and the superficial abdominal reflexes were absent.

By lumbar puncture a very small quantity only of cerebrospinal fluid was obtained, which was yellow and immediately coagulated on standing. The possibility of Froin's loculation syndrome occurring in osteitis deformans of the vertebræ has been mentioned by Greenfield, who cited the above case as an example. In his paper the microscopical appearances of a section of bone from one of the laminæ are shown, and are typical of those present in this disease.

Skiagrams of the upper dorsal region of the spine suggested the presence of a tumour at the level of the fourth and fifth dorsal vertebræ. In this area an irregular swelling appeared to project from the lateral aspect of the spine.

An exploratory laminectomy was performed by Mr. Percy Sargent. No tumour was seen, but the laminal arches were found to be definitely thickened. Pulsation of the cord was not at first apparent, and did not appear until the laminectomy was extended upwards beyond the level of the fourth dorsal laminal arch. At a later date the patient died, and for the following notes on the condition of the spinal column seen at autopsy I am indebted to Dr. J. G. Greenfield : " At the level of decompression the vertebral laminæ looked rather thicker than usual and were softer in cutting. Below this level the thickening and softening of the laminæ became progressively more marked, so that in the lower dorsal and upper lumbar regions the bone could be picked away by a dissecting forceps. The thickening of the bone caused the spinal canal to be narrowed so that the dura mater was everywhere in contact with the bone. It was also abnormally adherent to the bony arches all the way round. The cord was removed and appeared normal. At the lower part of the body of the eighth dorsal vertebra a small nodule projected backwards from the vertebral body, and a smaller nodule of a similar character was present on the body of the sixth dorsal vertebra. There was a depression of the anterior surface of the spine at the lower end of the tenth dorsal vertebra, as though the eleventh vertebral body had been displaced backwards. The body of this vertebra was reduced in depth. Below this level the contour of the lumbar spine was irregular. There was no evidence of thickening or bossing of the skull."

Both of these cases demonstrate the possibility of compression of the spinal cord as a result of the bony lesions of osteitis deformans affecting the vertebræ. The manner of compression is evident. Firstly, the increased thickness of the softened bones is not only productive of deformities on the external surface of the vertebræ but may also bring about a narrowing of the lumen of the vertebral canal. Secondly, the presence of bony excrescences projecting from the inner surfaces of the bones, as were found at autopsy in the second case, suggests an additional element in the production of compression. Two points in favour of the view that the spinal canal is reduced in size in such cases are afforded by the absence of the perithecal space and of the normal pulsation of the cord.

In both my cases the vertebral column was undoubtedly affected throughout the greater part of its length, but the encroachment on the spinal canal was not uniform, for there were in both cases symptoms attributable to local compression of the spinal cord. In neither case was there any external evidence of gross deformity, such as angulation or marked curvature, and spinal tenderness was absent. In the second case the bony changes typical of osteitis deformans appeared to be limited to the vertebræ.

By the kindness of Sir Arthur Keith, an opportunity was afforded, at the Royal College of Surgeons, of examining the vertebral column of a cadaver, in which the skull, facial bones, spinal column and many other bones of the body were extensively affected by osteitis deformans. Unfortunately with this specimen no clinical history was available.

The spinal column presented a moderate curvature of the dorsal vertebræ, with the convexity directed backwards, the lower dorsal vertebræ being the most prominent. From the second dorsal vertebra downwards a condition of osteo-fibrotic ankylosis of the spinous processes was present. In a macerated portion of the spine there was some lipping of the lateral edges of the bodies of the eighth, ninth and tenth dorsal vertebræ. Laterally the bodies of the ninth and tenth were almost fused over the intervertebral disc by this process. The intervertebral foramina were very unequal in size and many appeared to have been narrowed.

The spine was cut across at several levels. Alterations in the structure of the bone were most noticeable in the ninth and tenth dorsal vertebræ. The lumen of the spinal canal appeared distinctly small in comparison to the size of the vertebræ, especially in the lower dorsal region, the reduction in the dimensions of the canal being chiefly at the expense of its antero-posterior diameter. This diameter measured 12 mm. at the level of the ninth dorsal verebra. For contrast the antero-posterior diameter of the vertebral foramen was measured in the ninth dorsal vertebra from five normal adult skeletons and found to vary from 15·5 to 18 mm. While the transverse diameter of the canal in the diseased vertebra was 18 mm., this measurement varied from 15 to 18 mm. in the five normal vertebræ examined.

Inspection of the lumen of the canal formed by several normal vertebræ retaining their attachments to one another, showed throughout an evenly smooth surface. In the diseased spine, however, the inner surface both of the bodies and of the laminal arches was decidedly uneven. The greatest encroachment upon the canal was in the region of the laminal arches, due to the bulging inwards of their thickened superior articular processes.

The reduced size of the canal, its irregularity, and the lipping of the edges of the vertebral bodies, are well shown by the accompanying illustrations (figs. 1, 2 and 3).

Among the uncommon cases of osteitis deformans of the vertebræ, in which the presence of lesions of the spinal cord have been discovered, may be mentioned that of Marie and Léri. In this case a syringomyelic cavity was found to extend from the first cervical to the second dorsal segment of the cord. Subjectively the patient had complained of vertigo, and pains in the back and hips. Sensation, however, was stated by the authors not to have been grossly affected.

Gilles de la Tourette and Marinesco have reported the case of a man of 49, in which the skeletal tissues were widely affected, including the small as well as the large bones. During life the reflexes, the control of the sphincters and sensation were normal. Macroscopic and microscopic examination of the spinal cord revealed the presence of certain

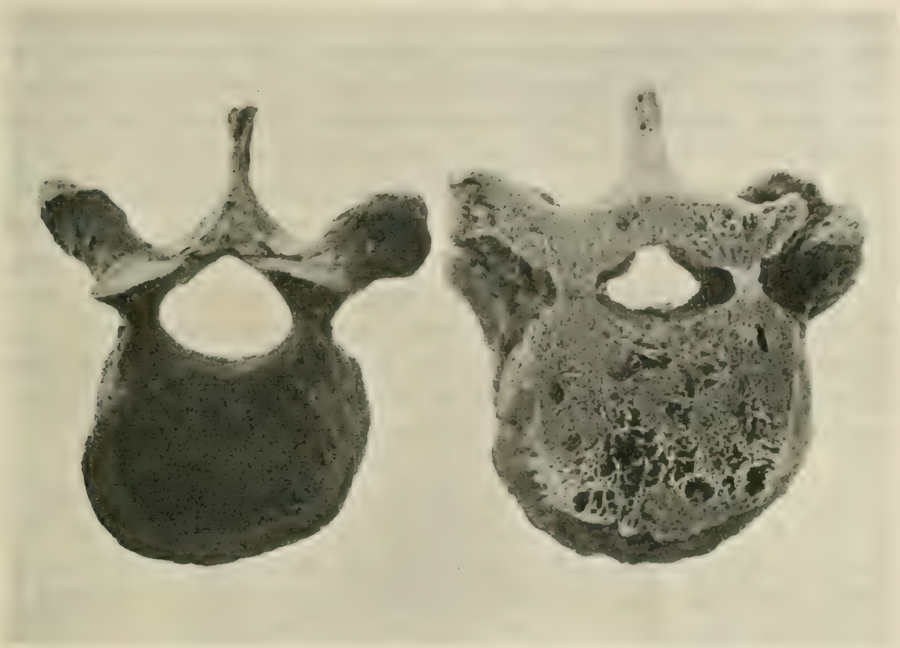

FIG. 2. FIG. 1.

In fig. 1 the lower half of the ninth dorsal vertebra of a case of osteitis deformans is shown. Rarefaction of the body with increase in size of the spaces between the lamellæ is conspicuous. In fig. 2 is seen a normal ninth dorsal vertebra for comparison. The difference in the lumen of the spinal canal of the two vertebræ is very obvious.

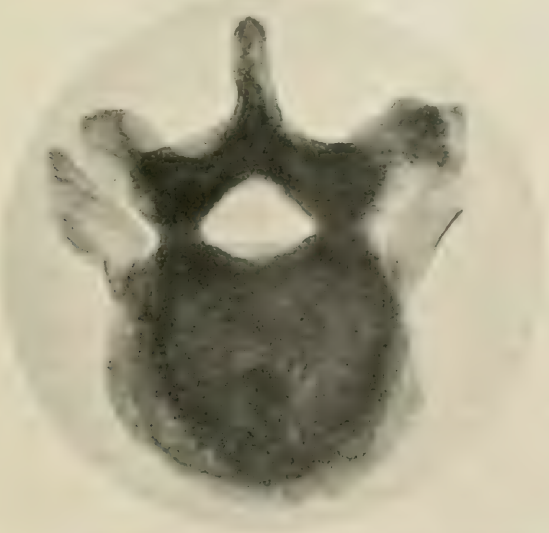

FIG. 3.—Skiagram of bone seen in fig. 1, showing rarefaction.

changes in the posterior columns and in the posterior part of the lateral columns, chiefly in the dorsal region of the cord. The cervical cord was not examined. These changes, slight in degree, consisted of an unevenly distributed rarefaction of the myelinated nerve fibres and of an increase in glial tissue. The anterior and posterior nerve roots appeared to be normal. It was suggested by the authors that the alterations in the bones were possibly of a trophic character, occurring secondarily to the changes in the cord itself, rather than the reverse. Several other cases have been described in which changes were found in the cord similar in nature to those mentioned in the above case. It is possible that such lesions represent the earliest effects of compression, before the gradual narrowing of the vertebral canal is sufficiently advanced to produce clinical signs of compression of the cord.

In the next two cases atrophy of the optic nerves was present in patients in whom the skull was affected by osteitis deformans. In both diplopia also occurred, indicating most probably an injury of one or more of the ocular nerves. Several of the long bones were involved in one of these cases, and the vertebral column in the other.

Case 3.—K. H., female, aged 61, was admitted December, 1922, under the care of Dr. Gordon Holmes. She had undergone an operation for polypus of the uterus at the age of 55. Her health otherwise had always been good, and both her parents had been healthy. She herself was married, but had had no children and no miscarriages.

At the age of 53 diplopia developed suddenly. The resulting visual confusion was sufficient to cause her to fall down on several occasions. Within a period of six months the diplopia disappeared. She had no headaches during that time. When about 55 years of age she began to suffer from "rheumatism or neuritis" in the right upper arm. These pains ceased at the age of 60. At this time, however, she noticed that the right humerus bulged forwards at its upper half. There never was any stiffness or limitation of movement at the shoulder-joint. At the age of 60 the sight of her right eye began to fail. She consulted Mr. Leslie Paton, who discovered signs of atrophy of both optic nerves. During the four months before admission the impairment of vision in the right eye increased rapidly.

The skull was large and appeared swollen and protuberant above the ears on either side. This bulging was more noticeable upon the right than the left side. The shaft of the right humerus was thickened and curved forwards in its upper half. At the right knee-joint the condyles of the femur appeared enlarged and measured more in diameter than those on the left side. She remembered an injury having occurred to the right knee-joint several years previously.

A lateral skiagram of the skull showed diffuse thickening of the frontal bone and an irregular uneven thickening of the other bones of the vertex. The bones at the base gave the appearance of having been pressed upwards in the region of the base of the sphenoid, conforming to the type of "convexobasie" of Léri. The dimensions of the pituitary fossa appeared to be normal. An antero-posterior skiagram showed well the extent of the bulging in the parieto-temporal regions.

The shaft of the right humerus was thickened and mottled in appearance, especially in its upper half, and there was rarefaction of the bone surrounding the glenoid cavity. Thickening and rarefaction were apparent of the lower end of the right femur, including the condyles.

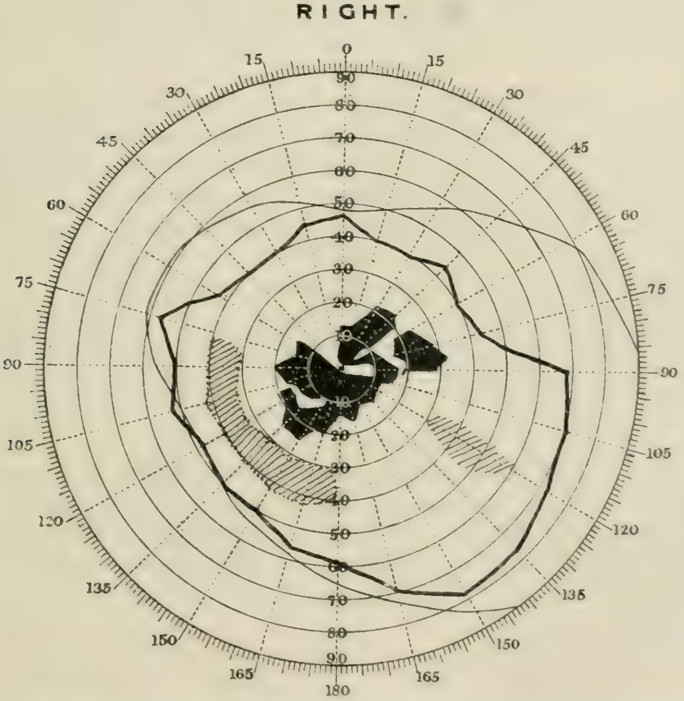

FIG. 4.—Visual field of right eye to a 10-mm. white object, showing central and paracentral scotomata. Colour vision retained at fixation point only. Central vision clear, peripheral vision indistinct.

Nervous system.—The visual acuity was $\frac{6}{12}$ in each eye. On ophthalmoscopic inspection the right optic disc was found to be pale all over, with a greater degree of pallor in the temporal than in the nasal half. The lamina cribrosa was visible. In the left disc there was pallor of the temporal half only. The edges of both discs were clear and the vessels of good size.

In the right visual field there was a large irregular scotoma which practically surrounded the fixation point, and a partial scotoma nearer the periphery in the inferior and nasal areas. Some constriction of the field was present, most marked in the two upper quadrants. The left visual field was full, and no evidence of scotomata was discovered.

The reactions of the pupils were normal. Hearing was considerably impaired in the right ear, conduction by bone being better than by air. In the left ear hearing, as tested by ordinary methods, was not affected. No other abnormalities of the cranial nerves were discovered. The Wassermann reaction of the blood and cerebrospinal fluid was negative, the cytology and protein content of the latter being also normal.

Case 4.—N. N., female, aged 52, was admitted September, 1923, under the care of Dr. Gordon Holmes. She had always been delicate. She had two children living, both in good health, while a third pregnancy had resulted in a "freak."

About four years previous to admission she suddenly developed double vision. This persisted for three months, and since had recurred for short periods. Soon after the onset of diplopia her sight began to fail gradually. Lately the visual impairment progressed more rapidly. She also became increasingly deaf in the last four years. Her height had gradually diminished by as much as 6 inches. It was noticed by her relatives that her head had become larger, and that her features had altered considerably in the last three years. These deformities passed unobserved by the patient until her attention was called to them. She was troubled with pains at the back of the head, and sometimes with a hot feeling over the vertex. For three months before admission she complained of pain at the bottom of the spine, and for some weeks of aching and stiffness of the right side of the jaw.

She was a short flabby looking woman with a slight stoop, and a large broad head sunk upon the shoulders, the chin almost reaching the upper end of the sternum. The lower limbs were separated unnaturally, rotated outwards and slightly bowed below the knee, with the feet turned out. The chest was narrow and the lower costal margins were almost in contact with the iliac crests.

The skull was broad and flat, and bulged at the sides so that the ears were tilted outwards; these were also turned slightly forwards by the enlarged mastoid processes. The back of the head was flattened, while the occipital protuberance was enlarged and lay at a much lower level than normal. The forehead was broad, low and slightly bossed upon the right side. In circumference the skull measured $23\frac{6}{8}$ inches (60 cm.). Both eyes were prominent, the nose sunken and the lower jaw prognathous, giving the features a somewhat froglike expression. Some fulness was present in the region of both temporomaxillary joints, and the movements of the jaw were restricted and stiff. The gums were edentulous. The hard palate sloped upwards and backwards from its anterior end. There was considerable rigidity of the spine, and the patient had great difficulty in raising the head to look upwards. Beyond some stiffness at the hip-joints, the movements of the limbs were unrestricted, and no thickening of the long or small bones of the extremities was observed.

A lateral skiagram of the skull showed that the bones of the vault were thickened everywhere, but particularly in the occipital and posterior parietal region. The outline of their external surfaces was vague and extremely irregular, while that of the internal surfaces was more definite, The frontal bone overhung the bones of the face, which were retracted with the exception of the prominent lower jaw. Posteriorly the most dependent part of the occipital bone was at a decidedly lower level than the foramen magnum, and the outline of the occipital fossa was angular in place of being curved. The bones in the region of the foramen magnum had the appearance of having been pressed upwards into the cranial cavity. The pituitary fossa was shallow, and the outline of the clinoid processes very blurred. A skiagram of the lumbar spine showed marked rarefaction of bone. Rarefaction was also observed in the region of the right hip-joint.

Nervous system.—The visual acuity of the right eye was $\frac{6}{24}$, and of the left $\frac{6}{15}$. Inspection of the fundi revealed pallor of the temporal halves of both discs, of slight degree in the right eye, more marked in the left. The edges of the nasal halves of the discs were a little hazy. The calibre of the vessels in both fundi was good, and no retinal changes were observed. No opacity of the lenses was present.

The right visual field showed considerable concentric diminution, while in the left field there was marked restriction of the temporal half, with moderate diminution on the nasal side. No evidence of scotomata, either partial or complete, was discovered. The fields of colour vision were markedly constricted.

The pupils were equal in size, circular, and their reactions brisk. The right external rectus and superior oblique muscles were completely paralysed, but diplopia was not present at the time of examination. Hearing was greatly impaired in both ears, the defect being of the middle-ear type. No other abnormality of the cranial nerves was present and the reflexes, sensory and motor systems, were normal. The mental state of the patient was rather feeble and her memory was much impaired. The Wassermann reaction of the blood was negative.

It appears permissible, by a process of exclusion, to assume that in these two cases of osteitis deformans the atrophy of the optic nerves resulted from their compression within the optic foramina. The state of the pupil reactions and the absence of any clinical sign of tabes dorsalis, in conjunction with the negative result of the Wassermann tests, were evidence against the condition being of luetic origin. The possibility of sinus infection could be set aside by the examination of the skiagrams of the skulls. The clinical histories failed to suggest the existence of any other possible cause of optic atrophy, whether toxic, infective or familial. Ophthalmologically the cases are of interest, for, as far as can be ascertained, osteitis deformans has not been previously included among the possible causes of optic atrophy.

By permission, an examination was made in the Museum of the Royal College of Surgeons, of two skeletons in which the skulls were affected by this disease. The optic foramina appeared to be reduced in size. In several normal skulls, a probe, roughly 5 mm. in diameter, could be passed with ease through the optic foramina, whereas in one of the affected skulls it became engaged in the walls of both foramina. In the other skull only one foramen could be penetrated by the probe. The capacity of the eye sockets was considerably reduced. This may explain the prominence of the eyes which is present in some cases of Paget's disease of the skull.

Ocular complications, however, are not uncommon in osteitis deformans. Paget himself, after an examination of twenty-three cases, reported that four had become blind; retinal hæmorrhages had occurred in three of these, and choroiditis was the cause of blindness in the fourth. The recurrence of retinal hæmorrhages has since been mentioned by numerous observers. These vascular lesions are more probably due to arterio-sclerosis, which is so commonly present in the subjects of this disease, than to vascular compression.

Coppez has reported four cases in which degenerative changes were present in the retinæ, in the macular and para-macular areas. In none of these cases could syphilis be held responsible for the disease in the fundi. Three cases described by Vergne all showed well-marked choroido-retinitis. In a case reported by Watson "high myopia with a large posterior staphyloma and extensive choroidal changes in each eye" were present. Numerous authors, such as Hurwitz, Vergne, Coppez and Vincent, have noted the presence of crystalline opacities in the lenses.

Paresis of ocular muscles has occasionally been observed in osteitis deformans of the skull. Diplopia developed in one of the cases described by Coppez, and had been present temporarily in the last two cases reported in this paper.

Deafness as a complication of this disease is fairly common. This may be due to compression of the auditory nerve, or, as was more probable in Case 4, to alterations in the bones, leading to disturbances in the sound-conducting apparatus.

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NOTICES OF RECENT PUBLICATIONS.

Lehrbuch der Nervenkrankheiten. Von H. OPPENHEIM. 7te wesentlich vermehrte und verbesserte Auflage. Zweiter Band. S.1389, mit 275 Abbildungen im Text und 9 Tafeln. Berlin: S. Karger. 1923.

The first volume of the new edition of Oppenheim's textbook on nervous diseases, which is now edited by Cassirer, Goldstein, Nonne and Pfeifer, was noticed in a recent number of this Journal. The second volume, which has recently appeared, has received even more additions, and though Oppenheim's original plan has been, wherever it was possible to do so, adhered to, there are many changes, and all of them, as far as can be seen on looking through the book, tend to improvement and completeness. There is a new section devoted to diseases of the basal ganglia, in which paralysis agitans, pseudosclerosis, Wilson's disease, double athetosis and chronic progressive chorea are included. The still indeterminate pathology of these conditions is carefully and on the whole fairly reviewed. The other chapters that have undergone most modification are those on the diseases of the fore-brain, in which epidemic encephalitis is now included; that on the neuroses, in which the recent work on the nature and origin of hysteria receives adequate attention, and that on the angio- and tropho-neuroses.

The type and the reproduction of the illustrations are excellent, the editing seems to be extremely efficient, and the very complete index at the end of the volume increases its value as a book of reference, and makes it almost indispensable to all workers in clinical neurology.

Miners' Nystagmus. First and Second Reports of the Medical Research Council Committee. London: H.M. Stationery Office. 1922 and 1923.

These reports include a summary of the primary conclusions of the Committee, a general report on miners' nystagmus, a report on the psychoneurotic symptoms associated with it, and sections on the incapacity resulting from the affection, and on the importance of errors of refraction in its pathogenesis.

The chief conclusion to which the Committee has come is that deficient illumination, due to the low illuminating power of the safety lamps and the great absorption of light by the coal, is the essential factor in the production of miners' nystagmus, They regard all other reputed factors as of little or no importance; they fail, for instance, to find any evidence that errors of refraction have an influence upon the disease. Their conclusions that the common belief among miners that there may be permanent damage to vision, or even total loss of sight if underground work is continued, is baseless, is obviously of great economic as well as of medical importance.

The section on the psychoneurotic symptoms of the disease suffers from the obvious lack of personal experience of the writer with the conditions he discusses and attempts to analyse.

Le Cerveau et la Pensée. Par HENRI PIÉRON. Pp. iv, 328. Paris: Félix Alcan. 1923. Price 10 fr.

More than one volume with a similar title and a more or less identical object to the book under review has appeared in the past, but to-day when our knowledge of the structure and functions of the nervous system is increasing rapidly, and in a period when psychology has become more objective and biological in its methods and has consequently thrown new light on the mode of working of the mind, the considered views of the Director of the Laboratory of Physiological Psychology at the Sorbonne cannot fail to be of interest.

This book, which belongs to "La Nouvelle Collection Scientifique," has been written for the layman rather than the specialist, but even the latter will find in it much of interest and instruction. The main thesis of the author is that before we attempt to interpret the functions of the brain in their relation to the functions of the mind, it is essential to understand the main principles at least of the physiology of the elementary nervous mechanisms; and that it is only when psychology approaches its problems from the point of view of the biological sciences, and especially of physiology, that it can attempt to solve or understand the nature of the mind.

Diagnostic et Traitement des Sciatiques. Par H. ROGER et G. AYÈMS. Pp. 164, avec 15 figures. Paris: Maloine et Fils. 1923. Price 8 fr.

This small book deals concisely but clearly with one of the commonest of nervous affections. The most interesting and valuable chapters are those in which the clinical features of true sciatica are contrasted with those of the "false sciaticas" where the pain does not arise from an affection of the nerve itself; with the symptomatic sciaticas, the term which the authors apply to painful affections of infective or toxic origin; and with the pains of sciatic distribution due to compression or other gross disease of the sensory roots or of the nerve.

A large part of the book is devoted to the treatment of the different forms of sciatica, and in this section even the most experienced clinician may find valuable hints.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

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BRAIN.

PART 4, VOL. 46.

SPEECH AND CEREBRAL LOCALIZATION.

BY HENRY HEAD, M.D., F.R.S.

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THIS work formed the basis of the Cavendish Lecture delivered before the West London Medico-Chirurgical Society on June 22, 1923. It contains a preliminary statement of the results to which I have arrived on the question of speech and cerebral localization. I hope to deal with the history, the clinical phenomena, and the anatomical data of aphasia more fully in book form, and have therefore ventured to omit all reference to the voluminous literature which has grown up around the subject. Nor have I referred to the valuable summaries of clinical reports contained in the book by Moutier [10] or in the three volumes compiled by Henschen [7]. I hope, however, later to collate my results with those of my predecessors.

CHAPTER I.—WHAT IS MEANT BY LOCALIZATION OF FUNCTION?

No one doubts that speech in its highest forms can be disturbed by destruction of the tissues of the brain, or that the manifestations differ according to the situation of the lesion. These crude facts have been habitually cited to prove the existence of "centres" for the various aspects of speech and an enormous literature has grown up around their supposed anatomical localization. But before it is possible to talk of "centres" for speech, we must first determine the nature of the functions that we believe to be "localized" in these particular areas of the brain, and consider what we understand by this expression.

Now the views as to the nature of these "centres" vary profoundly. According to a prevalent conception they consist of specially restricted depositions of cells which initiate and carry out those motor, auditory, or visual activities of which speech in its widest sense is composed. The surface of the brain is thought to be starred with a number of minute areas, each of which is responsible for initiating a specific act of motion or sensation; these are combined synthetically to form groups of functions of varying complexity. Each such "centre" has a definite position and function; like the push of an electric bell, it is fixed at one spot and produces a constant and predetermined effect.

§ 1.—"*Motor Centres*" *and Excitation of the Cortex.*

These mechanical ideas were based mainly on the results of electrical excitation of the cortex, particularly over the "motor" area. But they no longer appeal to more thoughtful experimenters, and the work of Sherrington and his colleagues on the anthropoid apes has shown how little such an interpretation is justified, even by the positive effects of stimulation. For the response from any one cortical point is not constant; it varies both in the nature of the movement evoked and in the part of the body thrown into action. The reaction depends not only on the site of excitation, but on the character of the events by which it has been preceded.

Successive stimulations of one and the same spot at short intervals of time usually produce definite facilitation and an increase in the amplitude of the response. Sometimes, however, the nature of the reaction changes; thus, a point, which began by yielding primary extension, may come to yield flexion in the latter part of a series of stimuli. This reversal, when it occurs, may appear slowly or, in some cases, develop with great rapidity; it may consist only of relaxation of the muscle, which was originally thrown into contraction from the particular cortical points; or there may be simultaneous contraction of its antagonist, previously the site of inhibition. (Graham Brown and Sherrington [2], p. 254.) Repeated or strong excitation of a flexor point often temporarily diminishes or suppresses the subsequent response of an extensor point; a similar increased resistance to flexion can also be produced, though less easily, from an extensor point. Even stimulation applied to the afferent fibres of a peripheral nerve, such as the ulnar, may have a profound effect upon the nature of the response subsequently obtained from a definite cortical area.

Graham Brown and Sherrington (p. 277) sum up as follows: "What we desire to stress in regard to the reaction of the cortical point on the antagonistic muscle-pair is the influence of shortly precurrent excitations, both of itself and of other points, and of afferent channels. And in this respect the functional instability of some cortical points seems to be greater than those of others. The instability is great enough to be easily demonstrable under narcosis as in our experiments. It may well be even greater in normal conditions without narcosis. Indeed, the frequency of reversal as a phenomenon attaching to the reactions of points in the motor cortex suggests that one of the functions of the cortex may be performance of reversals, and that the greater predominance of reversal under cortical than in purely spinal or decerebrate reflexes is because reversal is one of the specific offices of the cortex cerebri."

These ideas were developed still further in the remarkable paper of Sherrington and Leyton, published in 1917. Cortical motor points are functionally unstable and, during systematic exploration, three phenomena are liable to appear, all closely akin, "facilitation," "reversal" and "deviation" of response. For example, the whole anterior border of the motor field can be made to extend further forward by facilitation, and the area from which some particular movement can be obtained may be considerably enlarged. On the other hand, the nature of the response can be reversed either by repeated excitation of the same point, or by a previous stimulus applied to some part, which normally yields an opposite reaction. Deviation was exemplified by the following experiment, which I quote verbatim (p. 141) :—

"The examination of the motor area had in this experiment been begun at the top limit of the arm area in shoulder region, and proceeded systematically from point to point in the downward direction. Followed in this manner elbow flexion soon became the leading (primary) movement, and continued so very nearly or even quite down to the inferior genu of sulcus centralis. Beyond a certain point, which was minutely and precisely marked on the map made, elbow flexion disappeared abruptly, and facial movements appeared in the form of closure of opposite eyelids. The lower margin of arm area having thus evidently been reached, we turned to the delimitation of the face area. The examination of this area we started at the lower (Sylvian) end of sulcus centralis, and thence proceeded point by point upward along the precentral gyrus not far in front of sulcus centralis. In due course the point yielding closure of opposite eye was again reached, and it was found that then on proceeding farther upward to the point that had previously yielded elbow flexion as its primary movement, that point now yielded adduction of the thumb as its primary movement, and, a little farther upward, movement of index, chiefly extension, was added to that of thumb; and movements of thumb and index continued to be primary movements right up through the region which previously had given elbow flexion as primary response, and thumb and index movements as primary responses trespassed actually into the area that had previously yielded shoulder movements." Here "deviation of response" affected a series of points forming a considerable fraction of the whole arm area.

But this "deviation" could be produced in a still more remarkable manner. An electrical stimulus, applied to the post-central convolution, evoked no direct response in the anthropoid apes; yet it might profoundly influence the nature of a subsequent discharge from the motor cortex (Graham Brown [4]). Not only could it facilitate the response from adjacent precentral points, but even the form of movement evoked might be fundamentally changed by antecedent stimulation of an apparently "silent" area.

They conclude that phenomena such as facilitation, reversal and deviation of response, evidence of the functional instability of cortical motor points, are indicative of the enormous wealth of mutual associations existing between portions of the motor cortex. "The acquirement of skilled movements, though certainly a process involving far wider areas (cf. v. Monakow) of the cortex than the excitable zone itself, may be presumed to find in the motor cortex an organ whose synthetic properties are part of the physiological basis, which renders that acquirement possible." They add, "Such synthesis involves time adjustments as well as spacial adjustments." In fact, in the words of Franz, "the motor cortex is a labile organ."

These luminous experiments show the fallacy of conceiving the motor cortex as the seat of strictly limited "centres" of pre-ordained function. Cortical activity, even when aroused by electrical stimulation, is revealed as a march of events with a definite temporal relation. The response obtained from any one point, at a particular moment, depends on what has happened before. Excitation of a spot, which caused flexion of the elbow, may provoke the opposite effect if it follows some event, motor or sensory, favourable to extension. In the same way an area, associated at one time with contraction of the face, may yield movements of the elbow if approached from above downwards on the precentral gyrus. The past plays a predominant effect in the response obtained at any one moment, and this in turn helps to determine in advance the form of the future reaction.

These facts show that the "motor" centres cannot be the sole and primary foci from which movements are initiated. They form rather the means by which we are enabled at will to interfere with otherwise automatic acts. A series of high-grade movements are associated together in the acquirement of some aptitude, which, though at first learnt wittingly, ultimately becomes automatic. Cortical activity can then interfere with this series of actions and modify them in accordance with our voluntary requirements.

§ 2.—*The Effect of Cortical Ablation or Injury.*

Even complele ablation of one of these "centres" produces a transitory loss of function only, provided the injury does not extend deeply into the substance of the brain. Sherrington and Leyton ([8] p. 188) removed the whole area from which movements of the hand could be evoked by electrical stimulation. After recovery from the transient loss of power, the site of the injury was again exposed and stimulated without effect; the cortical tissues were then excised over a still wider area without producing any permanent or material change in the condition of the hand. Evidently the restoration of function was not due to the residue of a limited "hand area," which had escaped removal; nor was it the result of some vicarious activity on the part of neighbouring "centrès." But, after neural shock had passed off, the animal still possessed the power of re-learning an action which had been disturbed by the anatomical destruction.

Any change that may result permanently from the ablation of limited areas of the cortex is too subtle to be betrayed under experimental conditions by destruction of the so-called "motor centres," even in the anthropoid apes. But the afferent activities of the cortex stand in closer relation to consciousness than movement, and the condition of sensibility in man, after local injury to the surface of the brain, forms a better indicator of the nature of the functional disturbance.

We were able to show that the cerebral cortex is the organ by which we can focus attention upon the changes evoked by sensory impulses. A pure cortical lesion, which is not advancing or causing periodic discharges, may change the sensibility of the affected parts in such a way that the patient's answers appear to be untrustworthy. Such diminished power of attention makes estimation of a threshold impossible in many cases; uncertainty of response destroys all power of comparing one set of impressions with another and so prevents discrimination.

But in addition to its function as an organ of local attention, the "sensory" cortex registers and retains the physiological dispositions produced by past events. These profoundly modify all subsequent actions. They may be manifest in the form assumed by sensations or images, but more often, as in the case of spacial impressions, remain outside consciousness. Here they form organized models of ourselves, which we termed "schemata." Such schemata, although they may act solely on the physiological level, are essential for all accurate spacial recognition; for they modify the impressions produced by incoming sensory impulses in such a way that the final sensations are charged with a relation to something that has happened before.

The part played by the cortex in sensation is concerned with those physiological processes which underlie projection and discrimination. The loss of function appears in three forms, as inability to appreciate spacial relationships, defective reactions to stimuli of graduated intensity, and failure to recognize similarity or difference in objects of various shapes and weights. The crude qualitative aspects of touch, pain, heat and cold are not affected by a superficial lesion of the brain; they are functions of a subservient organ, the optic thalamus.

We saw reason to believe that these three aspects of sensibility were not always affected uniformly, or in any constant relation to one another by a cortical injury. Sometimes one group of tests, sometimes another, revealed a disturbance of greatest severity and widest extent. Such variation proves that the physiological processes, necessary for the due appearance of these different aspects of sensation, can be thrown into disorder more or less independently by lesions situated at different positions on the surface of the brain.

Moreover, I was able to show that the various portions of the body were not equally affected by injuries of the "sensory" cortex; those closely connected with the performance of conscious acts, variable at will, showed the most intense loss of function and could be disturbed from a wider extent of surface on the brain. Such parts as the hand, which are endowed with the greatest power of discriminative sensibility, suffered most severely; for the finger and thumb of man are little more than mobile sense-organs. Next in order came the sole of the foot, which habitually exerts discriminative activity in walking. The trunk is less likely to be affected, for the movements in which it is employed are mainly carried out automatically.

All cerebral activity consists of a march of events performed in part consciously, but to a greater extent unwittingly. On the physiological level the cortex undoubtedly plays a rôle in many automatic acts; but it also permits us to intervene to alter a sequence or to initiate some variation in accordance with circumstances. Thus, we are enabled to acquire with ease new aptitudes and facilities; once fully learnt, these in turn become more or less automatic. The deeper and wider therefore the injury to the cortex and underlying structures, the graver and more permanent is likely to be the loss of function; but we must never forget that it has disturbed a highly organized act and has not removed a strictly definable anatomical "centre."

Chapter II.—What Functions are disturbed by a Local Lesion of the Brain, which affects Speech?

Failure to appreciate the nature of the speech defects produced by local lesions of the brain has been responsible for much disappointment and waste of effort. A vast mass of valuable anatomical investigation has been rendered nugatory because the observer has been content to ecord the manifestations in general conceptual terms.

We are told in the clinical records that the patient was unable to speak, to read or to write; it is considered sufficient to note categorically that these acts were or were not possible, although in the vast majority of instances they could be carried out in one way, but not if the task was more severe or had been set in a different form. Thus a man may be able to write his own name and address, but not those of his mother with whom he lives. However careful the anatomical examination, cases are useless for the purposes of cerebral localization, where our only information is contained in the statement that the patient could not speak, read or write. Still worse are those where he is said to have suffered from "alexia" or "agraphia."

But even greater difficulties are encountered, if we consider the manifestations of aphasia under the headings of motion and sensation. Both physiological experiment and clinical experience show that destruction of parts of the precentral gyrus may cause loss of movement in the face and tongue. In the same way lesions of the occipital pole are followed by some loss of sight and those of the temporal convolutions by an affection of hearing.

Since normal exercise of the power of speech, in its widest sense, demands perfect movements of the tongue and the preservation of vision and hearing, these three functions were thought to form its constituent elements. It was assumed further that the products of disorganized speech would fall into the categories of motion and sensation. Aphasia was classified as "motor," "visual," or "auditory," and an anatomical site was sought for each of these varieties.

But innumerable clinical observations have shown that this is not the case. The negative effects of a cerebral lesion are manifested in terms of the function disturbed; loss of sensation of cortical origin is expressed as some defective form of the psychical act. Still more is this true of disorders of speech. They occur at a level of integration far above that of movement, or even of such specialized forms of sensation as vision and hearing; aphasia is manifested in terms of a group of functions I have called symbolic formulation and expression.

One and the same anatomical lesion can cause loss of function at diverse levels of cerebral activity. Thus, a cortical injury of the postcentral convolutions may produce not only gross defects in the highest aspects of sensation, but also diminution in muscular tone [6]. For, at this situation in the nervous system, the vital activity of the cortex is expressed in presentations to consciousness concerned with the position of the body in space and also in the purely physiological condition of tonic posture. Should a lesion of the left half of the brain be so situated that it causes loss of movement in one half of the tongue, it may at the same time be associated with some defect of speech. The want of power in the tongue is obviously a "motor" phenomenon; but the verbal disorders cannot be described under this heading. They belong to a higher order of integration. In the same way an injury to the hinder part of the brain may produce some form of cerebral blindness, accompanied by aphasic manifestations. Both are due to one anatomical lesion; but, whilst the loss of vision is truly "sensory," the defects in speech belong to a superior level of function.

Moreover, the conception that the various forms of aphasia can be classed as motor or sensory implied the fallacy, that cerebral destruction reveals the elements out of which an act of speech is composed. On this assumption, speech is analysed by the lesion into its synthetic components, as a salt is broken up into an acid and a base.

So long as we are dealing with the negative manifestations of a lesion of the central nervous system this is not the case. Positive phenomena, such as the spasticity of hemiplegia, or the over-response to painful stimulation which may follow lesions of the optic thalamus, reveal the activity of lower centres released from the control to which they are normally subjected. But as soon as we are concerned with purely negative manifestations, such as those of aphasia, the products of disintegration appear as some defect of a highly organized group of functions, all of which belong to the same level. No one is dominant or subservient to another; they are equipollent in the hierarchy of cerebral activities.

Speaking, reading and writing are highly developed actions, which have been acquired during the life of the individual. They are learnt with effort and constantly improved by practice. When they are disturbed by an organic lesion, the orderly march of a series of events is interrupted; the act of speech fails in one way or another, assuming different forms, just as a man's gait varies according to whether he has injured his toe or his heel. The necessary processes can no longer be carried out perfectly; but the particular form assumed by the disorder is the consequence of preventing in part the expression of certain highly developed functions and does not reveal the primitive elements out of which they were developed.

§ 1.—*Symbolic Formulation and Expression.*[1]

Most previous observers assumed that the perfect use of language in its various forms demanded certain activities of mind and body, and that these could be deduced by *a priori* reasoning on general grounds. These factors were supposed to form categorical groups, which were exposed by the disintegrating effect of disease, and thus, by examining the clinical manifestations, we could discover the synthetic elements out of which speech was composed. Some observers adopted as units the acts of speaking, reading and writing; others divided the phenomena into "motor" and "sensory," "emissive" and "receptive," whilst many were content with the purely descriptive terms of "apraxia" and "agnosia," which have no more explanatory value than the word "aphasia" itself.

Analysis of the facts of clinical observation has led me to fundamentally different conclusions; for, when a complex mode of behaviour, such as the use of language, is disturbed by structural disease, the loss of function is manifested in terms of the process itself and does not reveal the elements out of which it has been built up. Moreover, the various mental activities, interrupted during acts of symbolic formulation and expression, can frequently be exercised in a normal manner during some other form of behaviour. Thus the patient may have profound difficulty in manipulating visual images at will for the purposes of verbal expression, although he can employ them with ease in other modes of thinking. It is not images as such that are disturbed, but images used in a certain manner directed towards a definite end.

By symbolic formulation and expression I understand a distinct mode of behaviour in which some verbal or other symbol plays a part between the initiation and execution of the act. This comprises many procedures, not usually included under the heading of the use of language, and the functions to be placed within this category must be determined empirically; no definition can be framed to cover all forms of action, which may be disturbed at one time or another according to the nature and severity of the case. If clinical experience shows that some particular form of behaviour is affected in association with these speech defects, it must be included, although it is not logically implied in the purely descriptive term, "symbolic formulation and expression."

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[1] In my earlier papers I spoke of "symbolic *thinking* and expression." It was pointed out to me that this was too wide and indefinite a designation, and I have therefore adopted "symbolic *formulation* and expression" as more nearly approximating to my meaning and intention.

Since, then, it is impossible to define the exact limits of this group of functions, I shall attempt to enumerate shortly the various acts which may be thrown into disorder, when a unilateral lesion of the brain disturbs the use of language.

It is not the "general intellectual capacity" which is primarily affected, but the mechanism by which certain aspects of mental activity are brought into play. Behaviour suffers in a specific manner; an action can be carried out in one way, but not in another. In so far as these processes are necessary for the perfect exercise of mental aptitudes, "general intelligence" undoubtedly suffers. For a man who, in the course of general conversation, is unable to express his thoughts, or comprehend the full significance of words and phrases, cannot move freely in the general field of ideas. If, in addition, he cannot manipulate numbers with ease, or find his way from one place to another, he will certainly appear to be more stupid than his fellows. Moreover, it must not be forgotten that the intellectual life of civilized man is so dependent on speaking, reading and writing, that any restriction of these powers throws him back upon himself; he shuns company and cannot occupy himself with the newspaper or social intercourse. This inevitably leads to a diminished field of thought, and many aphasics gradually deteriorate in mental capacity. Yet closer observation shows that this "want of intelligence" is based primarily on some distinctive defect in a definite form of behaviour.

The more nearly the task approximates to a simple act of matching, the less does it suffer in those forms of defective speech on which this work is founded. All my patients could choose some familiar object, colour, or geometrical figure, which corresponded to the one shown to them. For in such tests the sensory pattern aroused by visual stimulation is matched with that produced by some one of the forms or colours on the table. No symbolic formulation intervenes of necessity between perception and the act of choice.

In the same way if one of the geometrical shapes or implements of daily use is placed in the normal hand out of sight, the patient can select its duplicate from amongst those on the table in front of him. Here tactile sensations evoke an image, which has obvious similarity with the visual impressions produced by some object within his sight.

But any act of mental expression which demands symbolic formulation tends to be defective, and the higher its propositional value the greater difficulty will it present. Thus a patient may execute a command to hold up his hand, although he is unable to carry out an order to touch with it his eye or his ear. The addition of the second factor has rendered it too difficult: the larger the number of possible alternatives presented by the task, the more certainly will the desired action be defective. By this means it is possible to grade the patient's disability. He is first required to carry out a series of movements such as "Lift your hand," "Shut your eyes," etc., which name one part of the body only. Then the right or left hand is specified, and the task is gradually increased in severity, until at last it is brought up to the multiple alternatives of the full hand, eye and ear tests. Somewhere on this ascending scale of difficulty the aphasic will break down, and this gives a rough indication of the degree to which this particular form of behaviour is affected.

Any modification of the task which lessens the necessity for symbolic representation will render its performance easier. Thus, a patient who finds extreme difficulty in imitating gestures accurately, sitting face to face, makes no mistake when they are reflected in a mirror; for this is in most cases an act of direct imitation. But, if instead of reproducing the movements he sees in the mirror, he is asked to write them down on paper, he falls into the grossest errors, because he is now compelled to express them in verbal symbols. Acts which can be imitated with ease cannot be formally expressed.

Many patients cannot find words sufficient for current speech or the accurate designation of objects; yet they can choose correctly both to oral and printed commands. For the verbal formula is presented to them ready made, and comprehension of its meaning is an easier process in such cases than the act of evoking it at will. Once the word has been presented to the patient, it calls up an image which corresponds to some object before him; but naming is impossible, because he cannot reproduce the adequate verbal symbol to demand.

The more abstract the symbol the greater difficulty does it present in cases where the use of language is defective. The words "knife," "penny," "match-box," are direct verbal symbols, appropriated exclusively to these objects by long familiar use. The names for colours, on the other hand, are more abstract; from the materials before us, consisting of paper, cloth or silk of different shape and texture, we abstract one quality which we call its colour. Thus many aphasics, who can designate correctly objects of daily use, fail when they attempt to find the names for colours.

On this principle we can explain the behaviour of No. 2, who, though unable to name colours, described them appropriately if he was allowed to employ a simile or metaphorical phrase. For example, when he failed to recall the name for "black," he described it as "What you do for the dead"; this he shortened to "dead," and could employ the single word to designate the colour because of its metaphorical significance, although he was unable to evoke the more abstract term "black."

It is a well-known fact that many aphasic patients, who are unable to write spontaneously, can copy printed matter in capital letters; in most cases this requires little more thought than imitative drawing. But to copy print in cursive handwriting is an act of transliteration demanding a certain degree of symbolic formulation. It is not surprising, therefore, that this form of behaviour is frequently disturbed, although it suffers less than spontaneous writing.

Sometimes it is possible to grade the extent of the patient's disability by means of these tests. He may be completely unable to write spontaneously, but does so, though imperfectly, to dictation, and can copy with comparative ease. For the last demands a relatively slight amount of symbolic formulation and expression, whilst to write spontaneously requires exercise of these powers to a high degree. But in some instances, especially if verbalization is mainly affected, copying from print may be gravely disturbed; like most normal persons, the patient glances at the words to be copied and then says them over to himself, as can be seen from the soundless movements of his lips. Copying from print becomes in fact a form of self-dictation and suffers from the same defects as if the words were dictated by the observer. In other forms of aphasia, however, copying is the least affected of all forms of writing.

The alphabet forms one of the most valuable means of investigating these defects in the use of language, provided the tests are carried out systematically. It is remarkable how many aphasics are unable to say the letters, or to write them in correct sequence, although they can repeat and write them to dictation. Under such conditions the patient not infrequently fails to construct an alphabet out of the twenty-six block letters; for he is unable to formulate them in due order.

It is comparatively easy to count and to say the days of the week, or the months of the year in sequence, provided it is possible to form the necessary words; long familiarity has made such tasks almost automatic. But to recognize immediately the significance of any single number, day or month demands a higher power of symbolic recognition. Thus, a patient who can count correctly and say the days of the week or the months may be unable to comprehend the meaning of a definite date such as "Thursday, March the twelfth." He is obliged to reach an understanding by recapitulating each series up to the word he is seeking to comprehend, just as he adds 6 + 3 by counting 6, 7, 8, 9.

The clock tests reveal a similar difference in the ease with which an order can be obeyed according to the nomenclature employed. A patient may be able to set the hands correctly at "3.40," but not when he is told to place them at "20 minutes to 4." For in the first instance he moves the short hand to 3, and then swings round the other consecutively up to 40 minutes; in the latter he sets the hour hand at 4 and then stops puzzled, in doubt as to the meaning of the words "20 minutes to."

These tests also show the existence of symbolic meanings that are not expressed in words or numbers. The short and long hands of the clock have acquired a significance which converts each of them into a direct symbol, and they are confused or used wrongly in many forms of aphasia. Moreover, we are in the habit of dividing up the space between any two numbers on the clock face into portions of an hour. Told to set "half-past one," we not only bring the long hand opposite to the figure 6, but we bisect the space between 1 and 2, and place the hour hand in this position. The interval between the two figures marking the hours has in itself a symbolic value. In many cases of aphasia this is affected, and the patient no longer sets the hour hand at a point proportionate to the position of the minute hand; he places the former opposite the figure 1, whilst the latter indicates 6. Or, more confusing still, when told to set "a quarter to six," he may place the short hand at 6 and the long hand opposite 9, so that it is impossible to discover without questioning him whether he intended to set 6.45 or 5.45. Not only the hands of the clock, but their relative position on the face has acquired a symbolic value, which is disturbed in many cases of aphasia.

Recognition of the passage of time and of its intervals is not strictly affected. A patient may be unable to tell the hour set for him on the clock, although he has a definite appreciation of the time of day and is punctual for his appointments. Even though he fails to name the hour, he may describe it correctly as "when you eat" or "when we went there."

In the same way sense impressions can be appreciated and recalled, but the aphasic may find difficulty in expressing the relation between them. Thus, when tested with the compass-points, he may be unable to answer in speech or writing whether he has been touched by two or one, although he possesses the necessary words to do so; and yet we can prove that his sensibility is not affected. For, if the figures 1 and 2 are written on a sheet of paper, he may by pointing be able to indicate correctly whether the contact was double or single. When this test is carried out in the ordinary manner, he is compelled to formulate his sensory impressions and express their relation in suitable words. But by the second method the processes of thought required are simpler; he has only to match the image produced by his afferent impulses with one of the two verbal patterns in front of him.

To the functions of the superior cerebral centres we owe predominantly our capacity to appreciate the various qualities and relations of external objects. By the time man developed speech, he already possessed the power of discrimination to a high degree, and definite symbols, such as words and numbers, were invented to register these differences.

When we are shown a coin and are allowed to handle it, we receive certain sensory impressions; these we abstract from it and speak of them as its objective characters. It is hard, brown, cold, round, of a certain size and is commonly called a "penny." But, in addition to these sensory attributes, it has other relations such as its position in space with regard to its surroundings. Place a set of familiar objects or colours on the table and ask the patient to point to the duplicate of one he has just seen; he not only chooses correctly, but after a time his finger will move at once towards the position of the object he wishes to indicate, even though the whole set is still screened from his sight. But as soon as he is asked to formulate the order in which they lie on the table, that is their serial relation to one another, he may fail completely.

In the same way a patient with his eyes closed may be able to point to the position of various objects in some familiar room with regard to himself, although he cannot formulate their relation to one another. He can say "The window is there, the fireplace there," but is unable to express the situation of the one with regard to the other. This makes it impossible to draw a ground plan, which demands somewhat complicated acts of symbolic formulation.

But such an object as a coin has a still further relation to others of the same order, namely, its monetary value. If two coins are placed on the table, many aphasics are unable to state how many of the one would be required to correspond with the other; given a sixpence and a two-shilling piece, they fail to reply that four of the one "go into" the other. Yet from a number of pieces of money they can build up a pile on the one hand, which exactly corresponds in value to the two shillings on the other. It is not appreciation of monetary value that is at fault in such cases, but the power to express the relation of one coin to another. In the same way No. 10 remembered that, when buying tobacco he placed two shillings on the counter and received two ounces and threepence in change ; but he was unable to say how much it cost. He could register the facts of the purchase correctly, although he could not relate them to one another and draw the obvious deduction.

Another form of activity, which is more particularly disturbed in a certain group of speech defects, is what may be called the ultimate intention of the symbol. Some patients have no clear or certain conception of the goal of an action they are asked to perform. This is profoundly evident in all that concerns words and figures ; but it is not the individual words in their primary sense which are affected. No. 10 understood the meaning of " summer " and " time " ; he was well aware that with the advent of " summer-time " the clocks were changed, but he was entirely unable to say whether the hands were put forward or back, and tried in vain to work out the problem. Such patients cannot add or subtract with certainty ; they have lost their knowledge of the processes of arithmetic, but not of the direct significance of figures.

This failure to formulate the intention or ultimate goal of a desired action leads to loss of capacity to perform tasks not directly associated with words and figures. Thus, when No. 10 was threading a quadrilateral frame for his beehives, he could carry out the operation if the action consisted in bringing the wire across from one side to another, and then back again through neighbouring holes ; but, as soon as he attempted to go from corner to corner, he failed entirely. He could carry out a strictly consecutive action, but found difficulty when he was compelled by the discontinuity of the task to formulate his intention. Such patients cannot collect the various objects they require for shaving and may fail to lay the table correctly for breakfast. All such games as billiards and cards become impossible, because of the difficulty in formulating beforehand the aim or goal of some particular act.

I have attempted to describe shortly the various actions which may suffer when " symbolic formulation and expression " are affected. It is impossible to find any single term to include all these disorders of behaviour, which extend on the one hand from mechanical aptitudes to exercises in formal logic on the other. I therefore chose an empirical designation to indicate that the defects produced by the lesion are manifested most often and most profoundly in the use of words, numbers and other analogous symbols.

§ 2.—*Specific Varieties of Aphasia.*

This group of functions is not uniformly disturbed in every instance and cases of aphasia differ profoundly in their clinical manifestations. The majority, especially in the earlier stages, show evidence of widespread defects in the use of language; the more acute and severe the lesion, the graver and more extensive is the disorder it produces. Many of these changes may disappear, and sometimes the patient recovers entirely; but in certain cases one or more aspects of symbolic formulation and expression remain affected, and the aphasic manifestations consequently assume some particular form.

Analysis of these clinical varieties seems to show that the various forms of behaviour, included under the term symbolic formulation and expression, can be affected in different ways in consequence of organic injury. These diverse defects of speech do not reveal the elements out of which the use of language is built up; on the contrary they show the way in which a highly complex series of acts can be disturbed by lesions of certain portions of the brain. Provided we bear these principles in mind, we are justified in grouping the clinical manifestations under separate headings. Fortunately, all the functions included under symbolic thinking and expression are rarely lost in the same patient; for, if this were the case, he would be reduced to a state in which all detailed examination was impossible.

To each of these groups I have given a name chosen from the most salient defect in the use of words; these names are purely indicative and are not intended in any way as defining a specific set of psychical functions.

(*a*) *Verbal Defects.*

In severe forms of this disorder the patient's utterance may be reduced to "yes" and "no," and even these words cannot always be evoked for voluntary use. As speech returns his vocabulary increases, but his enunciation is slow and halting. Any word he is able to recall can, however, be used for naming an object. It may be so badly pronounced as to be scarcely recognizable, but it is applied correctly. When the patient attempts to repeat what has been said to him, the articulatory sounds are imperfect, although he can usually utter more words than he can produce spontaneously. It is characteristic of this form of aphasia that words are evoked with difficulty, and tend to be abnormal in structure.

After the stage of neural shock has passed away, comprehension of verbal significance is rapidly restored; the patient can not only choose an object to oral or printed commands, but even complex orders may be executed correctly.

The power of reading to themselves with enjoyment is spoilt by difficulty in remembering a series of words accurately; they are frequently compelled to look back to the beginning of a long sentence in order to obtain its full meaning.

As the spoken vocabulary increases the power of writing is regained, although throughout it tends to show the same errors as articulatory speech. These patients cannot spell, and find difficulty in remembering the order of the letters, even in simple words. They write more easily to dictation, but are unable to carry in the memory a string of words or a long phrase.

The verbal aspect of numerals is affected, but not their significance. Thus, when looking up the page of a book or scoring at cards, the patient may utter the wrong number, but acts as if he had said the right one. Simple arithmetical operations can be carried out correctly, except in severe cases; then it is not the process of addition and subtraction which is forgotten, but the act fails because of the difficulty in remembering the requisite figures.

These patients can draw, play card games and enjoy jokes set out in print or pictures. In fact, the disorder from which they suffer affects mainly verbal structure and words as integral parts of a phrase; their nominal value and significance are perfect.

(*b*) *Syntactical Defects.*

This is an easy form to distinguish, because the patient tends to talk jargon. Not only is articulation of the words ill-balanced, but the rhythm of the phrase is defective, and there is a want of grammatical coherence. The power of naming objects may be retained in spite of the jargon by which he is hampered. Not infrequently, when he cannot utter some word, or when the sound emitted is incomprehensible to his auditor, he writes the name correctly.

Comprehension of the meaning of words is always in excess of their use in conversation. These patients can choose common objects or colours without fail to oral commands in the form of a single word; if however, the order is conveyed in a spoken phrase it may not be understood correctly. In daily intercourse they suffer from inability to recall with certainty what they have been told ; not only is phrasal utterance defective, but phrasal memory is transitory. This makes consecutive conversation difficult or impossible.

Such patients can understand what they read to themselves, provided they are not compelled to reproduce the meaning in words ; for their internal speech is also disturbed by jargon.

Single words may be written correctly ; but any attempt to convey a formulated statement in writing is liable to end in confusion. Patients suffering from the more severe degrees of this affection cannot write a letter ; but in slighter cases writing is easier than articulatory speech and all can copy correctly, transcribing print into cursive handwriting.

This disorder is essentially one of balance and rhythm in symbolic expression, and syntax suffers greatly. The patient has plenty of words, but their production is ataxic ; this leads him to talk jargon and renders difficult even internal formulation of their meaning.

(c) *Nominal Defects.*

This is essentially a loss of power to use names and want of comprehension of the nominal value or meaning of words and other symbols. Not only does the patient fail to name objects placed in front of him, but, when asked to point to one of them named aloud or in print, the choice, even if correct, is made slowly and with effort.

Such patients read with extreme difficulty, especially if they attempt to spell out the words. Writing is gravely affected and although they can copy printed matter correctly in capitals, they may be unable to do so in cursive handwriting. Writing to dictation together with all actions demanding choice are carried out imperfectly to spoken commands ; but direct *viva voce* repetition is not affected.

They can usually count and say the alphabet, but suffer from defective appreciation of the meaning of single numbers or letters. This interferes with the power to carry out simple arithmetical operations, and appreciation of the relative value of coins is usually more or less affected. Games, such as cards, which demand rapid and correct recognition of names and power to register a score, are impossible, though chess, draughts and dominoes may be played correctly.

Drawing from a model, or from memory after the object is removed from sight, is easily performed; but, when the patient is asked to draw some such figures as that of an elephant from imagination, the result is extremely unsatisfactory. All the distinctive parts are usually omitted.

One of the most instructive forms, assumed by the loss of function, is the difficulty experienced by the patient in producing a ground plan of some room with which he is familiar. However badly the verbal aphasic may draw, he usually succeeds in indicating the relative position of the windows, doors and principal pieces of furniture. But the patient with nominal defects fails to produce a correct plan, and tends to slip into an attempt to express the constituent parts in elevation; yet when asked "Where is the table?" or "Where is the window?" he can point to their situation correctly.

(*d*) *Semantic Defects.*

These consist in a want of recognition of the full significance of words and phrases apart from their verbal meaning. Other functions suffer that have nothing to do with verbalization; for in this form of disorder there is loss of meaning in consecutive thought. The patient may understand a word or short phrase, and can appreciate the various details of a picture; but the ultimate meaning escapes him. Thus, although he understands the significance of the words "summer" and "time," and knows that "summer-time" is "something to do with the Daylight Saving Act," he is unable to say whether the clocks are put forward or back when it begins.

He fails to comprehend the final aim or goal of an action imposed upon him from without. He cannot formulate accurately, either to himself or to others, a general conception of what he has been told, has read to himself, or has seen in a picture, although he can enumerate many of the details of which it is composed; the knowledge he has gained is episodic. Such patients can read and write, but the result tends to be inaccurate and confused.

Counting is possible, and the value of numerals and of coins may be recognized; but arithmetical operations are affected from want of appreciation of the nature of the procedure required.

Such patients fail to understand jokes which demand complete comprehension of printed words or pictures. They cannot play card games or put together puzzles, which confuse them greatly.

These semantic disorders interfere seriously with the activities of daily life and render the patient useless for any but the simplest employment; and yet his memory and intelligence may remain on a comparatively high general level. He does not forget people or places; he can recall spontaneously events both recent and remote, and may be able to give valuable information with regard to his disabilities. But, if he is set the task of retailing accurately some story which he has been told or has read to himself, he is liable to become confused and to omit many factors of importance.

§ 3.—*The Effect produced by the Degree of Loss of Function on the Form assumed by an Aphasia.*

Of the many aspects of behaviour, comprised under the term symbolic formulation and expression, some are affected in one case some in another, and the form assumed by the clinical manifestations depends primarily on these qualitative defects. But the characteristic changes also vary profoundly according to the amount to which any one group of functions is disturbed. At first the patient may be unable to speak, to read or to write; but with the lapse of time he may regain sufficient power to carry out all these actions, and yet the manner in which they are performed shows that he is still suffering from the same specific variety of aphasia.

The quantitative aspect of these disorders of speech, on which von Monakow has so repeatedly insisted, has been almost universally ignored. The question is asked, "Can the patient understand what is said to him, can he speak, read or write?" and he is placed in one or other group according to the answer. Each such categorical combination of signs and symptoms is then erected into a "morbid entity" or "syndrome" (e.g. "alexia" or "agraphia") and attempts are made to associate it with some structural change in a particular part of the brain.

No records are obtained of the depth of the specific affection by means of tests of the same order but of graduated difficulty. I have already given examples to show that a patient can exercise some particular aptitude in a simple form, but fails to be able to do so if the task is rendered more complex. Thus it is useless to assert only that he could speak, read or write; we must inquire, with the help of graduated tests, how much power he has of performing these acts.

Moreover, it is a fundamental error to look upon the clinical manifestations at any one moment as if they were permanent and could be directly associated with demonstrable anatomical changes in a restricted area of the brain. The condition of the patient is not static; from the physiological point of view every case must be regarded as a disorder of function, which is in process of changing. It is either increasing or decreasing and the extent and severity of the aphasia may fluctuate from time to time.

Most patients who come to post-mortem examination are for this reason entirely unsuited for the purposes of anatomical localization. They suffered from some progressive disease of the brain and the clinical signs were profoundly influenced by the widespread functional effects of diaschisis.

On the other hand, if the lesion remains completely stationary and mental and physical vitality are high, the power to use language returns to a remarkable degree. Quiescent anatomical changes are associated with a gradual restoration of function.

But anything which causes neural shock, such as an epileptiform attack, or even the lowered vitality consequent on fatigue or worry, profoundly reduces the power to use words. This may pass away so rapidly that it cannot have been due to any variation in the gross structural changes.

By bearing these principles in mind we are able to compare the severity of the disturbance of function in any two patients belonging to the same class of aphasia and to determine the degree of recovery or deterioration in a single individual at different periods. Because a man, who was unable to read or write, regains his power to carry out these acts, there is no reason to suppose that the situation or extent of his cerebral lesion has changed materially. The clinical manifestations may have altered in character solely in consequence of the diminished degree to which some particular language function is affected.

(*a*) *A Case of Acute Verbal Aphasia followed through various Stages of Recovery.*

The following example illustrates the effect produced on the manifestations of verbal aphasia by the acuteness and severity of the disturbance. So little permanent injury was produced in this patient by an operation for the removal of an intracranial tumour that recovery of function was rapid and could be recorded by means of graduated tests.

The patient (p. 430) was a middle-aged woman, who for six years had suffered at rare intervals from seizures beginning in the right hand; six of these were sufficiently severe to be accompanied by loss of consciousness. From time to time she had also had slighter attacks, which began with a " numb feeling " in the right thumb followed by involuntary flexion of all the digits. On May 20, 1922, she experienced these symptoms without loss of consciousness; but, after the seizure was over, she was alarmed to find that she could not speak for several hours.

Ten days later, when she first came under my observation, speech was perfect and I could find no abnormal physical signs of any kind except loss of the reflexes over the right half of the abdominal wall.

At the operation, on June 20, a smooth, lobulated growth was exposed springing from the dura mater on the left side; this had severely indented the substance of the brain in the region where the inferior frontal meets the precentral fissure. It was so carefully extracted by Mr. Wilfred Trotter that not the smallest fragment of cortical tissue adhered to the tumour after removal.

This operation was followed by complete verbal aphasia and flaccid right hemiplegia, accompanied by the usual changes in the reflexes on the affected half of the body. At no time was sensation in any way affected.

She improved rapidly day by day both physically and in her powers of speech. Her general condition was so unusually good that I was able to follow her recovery by means of serial tests, which yielded invaluable records illustrating the relation to one another of the various acts of verbal formulation and expression and of the order in which they were restored.

At first she was speechless except for "yes" and "no," and even "no" was at times wrongly employed. She seemed to understand simple orders, but frequently failed to comprehend the full significance of questions and was profoundly puzzled by her inability to express her wants. Told to touch her nose or give her hand she could do so, but became confused if I specified the right or the left.

When tested on the seventh day with a set of familiar objects in the usual way, she could point to the one on the table which corresponded to that she had seen or held in her hand out of sight; the act of matching was evidently performed with ease. She also chose correctly, though more slowly, to oral commands and made two mistakes only, when the order was given in the form of a printed word. She named these objects in ten out of eighteen attempts and most of her failures were due to defective word formation; for the sounds she uttered bore an evident relation to the names she was seeking. When she attempted to write them down without saying them aloud, writing and spelling were defective; and this was the case even if she copied the words from print. But she was able to repeat them after me, although her articulation was imperfect. Three weeks later all these tests could be carried out, but she still had difficulty in writing down the names of objects shown to her; each word corresponded to the usual nomenclature, but the spelling was poor and the letters were badly formed, Four months after the operation she could write the names perfectly; but this test was the last of the group to show complete recovery.

The alphabet formed a most instructive guide to the order in which her powers of verbal formulation and expression were restored. On the seventh day after the operation she could not say the letters in proper sequence, but repeated them after me and read them aloud correctly. If she attempted to write them down without saying them aloud, many were badly formed and the order was imperfect. Even when the letters of the alphabet were displayed before her, she tended to copy them in capitals and could not translate them into cursive script.

Ten days later she said the alphabet without a mistake. But, when I gave her the twenty-six block letters and asked her to arrange them in order, she was unable to do so; and yet she could read them perfectly aloud. She transcribed printed capitals into cursive handwriting very imperfectly and wrote the alphabet badly even to dictation. Improvement steadily continued and four months after the operation she could execute all these tests, although, when she wrote spontaneously or copied the letters, they still showed slight defects of form.

The hand, eye and ear tests not only gave an insight into the nature of her defect but admirably illustrated the mode of her recovery. At first, although she obviously understood simple statements, she was liable to become confused if the words implied an order. She could touch her nose with her right or left hand, but, when asked to bring one or other into contact with either the eye or the nose, she frequently failed to do so.

On the tenth day after the operation I was able to carry out a more complete series of tests on these lines. There was no question that she now understood in general what she was asked to do; but a series of oral commands to touch one or other eye or ear with the right or left hand were imperfectly executed. When orders were given in print, she failed to exactly the same extent.

She had not the slightest difficulty in imitating these movements made by me, if they were reflected in a mirror; this is an act of almost pure imitation as far as this form of aphasia is concerned. But sitting face to face she failed in eight out of sixteen attempts. Asked to describe my movements in writing, she was unable to do so; she put down right or left to correspond to the hand I had used, omitting all indication of which eye or ear I had touched. Moreover, the words were badly formed and, towards the end of this series, her writing became illegible.

The first of these tests to show recovery was her response to oral commands, which were correctly carried out twenty-six days after the operation. At this time printed orders were imperfectly executed. A week later the only forms of this test in which she failed were imitation of my movements, sitting face to face and writing them down on paper. Four months after the operation the latter task was the only one that was not performed correctly.

I have selected these three groups of tests for comment, because the records were characteristic of the mode of recovery; all the other serial methods yielded similar results. Each task suffered according to the degree of verbal formulation and expression required for its accurate performance. Simple matching was carried out perfectly throughout; she chose with ease the object corresponding to one she had seen or held in her hand and set one clock in accurate imitation of another. Oral commands were executed slowly; she chose familiar objects correctly, but made many mistakes with the more complex hand, eye and ear tests. The power of doing what she was told was the first to recover, because orders given by word of mouth demand little spontaneous verbalization; the words are pronounced by the observer and the patient has simply to remember them long enough to execute the movements required. Next in order of difficulty, and therefore of recovery, came translation of printed commands into action; for here the words must first be deciphered before they can form an effective order. Imitation of movements, when observer and patient sit face to face, demands a considerable degree of accurate verbal formulation, even though no word is spoken; this test was therefore severely affected and was not correctly carried out until a late stage of recovery. To write down such movements implies a still greater power of symbolic expression and was imperfectly executed even four months after the operation. In fact writing showed the most persistent defects, apart from those of enunciation.

In spite of rapid and profound recovery of articulated speech these abnormalities in verbalization were still obvious to the end. She talked easily, her pronunciation was greatly improved and the pauses occurred at longer intervals; yet, in principle, the defects were of the same kind as before and she was conscious that her speech was still lacking in freedom.

In this severe example of verbal aphasia the acts of speaking, reading and writing were all affected at first; even the power of understanding what was said to her was somewhat disturbed. As she regained her capacity to use language, those aptitudes returned first which were least dependent on accurate word formation. To the last, however, although she recovered her power to speak, to read and to write, she remained a characteristic instance of verbal aphasia. For it is evident that the slight difficulties in articulation and in writing which remained resulted from a want of facility in verbal formulation and expression. Clinically she had been transformed from a severe example of this disorder into one so slight, that it might have been mistaken on less complete examination for an articulatory disturbance only.

The course assumed by the recovery of function in this case is a striking confirmation of von Monakow's description of the order in which the symptoms pass away in what he calls "motor" aphasia ([9] p. 591). First, internal speech becomes freer and the comprehension of spoken or written words may return completely. Then the loss of power to evoke words ("dumbness") yields gradually; the patient learns to utter those in common use and can repeat them to order. But speech is uncertain, the voice monotonous, intonation defective, syllables are slurred and there is a tendency to perseveration. Emotional expressions are uttered with greater ease and certainty. Then follows a period in which short sentences evoked spontaneously and words in common use can be said without difficulty; at this stage the patient may remain for many weeks or months.

It is interesting to notice that the physical signs followed the same rules of recovery as the aphasia. Those parts which stood least in direct relation with the injured parts of the brain were the first to recover; thus, power returned to the lower extremity within four days, whilst the movements of the right angle of the mouth were not restored until a fortnight had elapsed. The last to become normal was the reflex from the lower half of the abdomen on the right side, the only sign that was defective before the operation. On the other hand it is an important fact that sensation was never affected even at the height of the hemiplegia; for no sensory functions stand in direct or indirect relation with parts so far forward in the brain as the site of the primary lesion.

(b) *Other Examples of the Clinical Varieties assumed during Recovery.*

It is seldom that opportunity occurs to watch recovery step by step from so acute and severe a form of aphasia. But several of my patients with gunshot wounds of the head showed profound improvement in their capacity to perform the various tests during the period they were under observation. Each different disorder of language led to some distinct and characteristic form of abnormal behaviour; but the clinical manifestations varied greatly, in cases belonging to the same specific group, according to the amount of the disturbance of function.

Shortly after the injury the patient may be grossly aphasic and unable to execute the serial tests without mistakes. With return of power, the records steadily improve and finally recovery can take place to such an extent that he is able to speak, to read and to write. But, in spite of this profound restoration of function, defects are still evident which betray the nature of the original aphasia; the patient is conscious that he cannot perform all acts of language with normal ease and at the same time the observer notices a definite lack of freedom in some aspect of symbolic expression. The characteristic disorder is still present to a minor degree.

Each specific form of aphasia depends on a predominant disturbance of certain aspects of symbolic formulation and expression. As recovery occurs those functions are first restored which have suffered least, and in this way it is possible to obtain a further conception of the essential nature of each variety of disorder of speech. Moreover, it is only by watching the various stages of recovery that we are enabled to understand those "partial" cases, where the defects in the use of language were slight from the beginning. I shall therefore select one example from each group to illustrate the changes in the clinical picture produced by recovery, or by diminution in the severity of the affection.

(1) *Verbal aphasia.*—No. 6 (p. 447) was at first speechless and silent; he could not even utter "yes" and "no." But his power of finding words rapidly improved and, in less than a month after he was wounded, he could say the alphabet and the days of the week, although both letters and words were extremely badly pronounced. An attempt to give the months in order led to a string of incomprehensible sounds.

He understood what was said to him and commands requiring a single choice were carried out accurately; thus, he had no difficulty in putting out his tongue, shutting his eyes or giving his hand, when asked to do so. But, as soon as two of these orders were combined, his response became hesitating and he was liable to fall into error.

Given a newspaper, his comprehension of the printed phrases was obviously defective; he could, however, reproduce accurately the simple words of the man, cat and dog test.

He wrote his name and address, but, when asked to direct a letter to his mother, with whom he lived, failed completely. Writing was grossly affected and, although he showed considerable power of putting down on paper what he had seen, in the form of single words, he was unable to write consecutively. Simple phrases were badly written to dictation, but he could copy them from print in cursive handwriting.

This severe degree of aphasia rapidly passed away, and seven months after the injury he had already recovered considerable powers of speech. Verbal formation, still obviously defective, was betrayed by faulty enunciation and spelling. When he attempted to say the alphabet spontaneously, many of the letters were mispronounced and the order in which he gave them was incorrect; similar faults appeared in writing, and he could not even construct a complete alphabet out of the twenty-six block letters.

It is not surprising that writing in general was gravely affected; the form of the words was faulty and his errors in spelling followed the same lines as his defective utterance. In fact, spoken words and written speech showed the same kind of faults.

Throughout all the tests, simple or complex, he was able to carry out oral commands; for, during this method of evoking a choice, the word is presented ready formed by the examiner. No verbal formulation is necessary on the part of the patient; he has but to understand and to act accordingly. With printed commands the task is not so simple; he is compelled to read the words before he can convert them into an effective order. Thus, although he chose common objects or colours and set the clock correctly, he failed with the more complex choice of hand, eye and ear.

Seven years later he had regained his power of carrying out all the serial tests perfectly, except that his spelling was faulty; but he still remained a typical example of verbal aphasia. He hesitated in finding words to express his thoughts, the pauses were unduly frequent and prolonged, and enunciation was defective. He could read aloud intelligibly, but stumbled over the longer words and complained that, when reading to himself, he was obliged to go over the same passage twice before he could grasp its meaning. For, as he said the words to himsel silently, he was liable to mispronounce them, and this confused him and destroyed his fluency. In the same way, although he could write an excellent letter unaided, he was slow and required "plenty of time." Asked to read a short paragraph and to put down on paper what he had gathered from it, he produced a coherent though somewhat shortened account; he was able, however, to say definitely what he had omitted. The sequence of ideas and grammatical structure were good; but he wrote slowly and with obvious effort.

The only tests which still gave a definitely abnormal result were those with the alphabet. Asked to say the letters in order, the sequence was defective, he wrote them imperfectly, and even hesitated in putting together the twenty-six block letters. But he could read them aloud, repeat them after me and write them to dictation.

This patient was a characteristic example of want of capacity readily to formulate or express thought in words. Articulated speech, and particularly writing, suffered severely, because they demand accurate verbalization; they were the last acts to recover, and were still defective seven years after the injury. In the earlier stages repetition was disturbed because of the difficulty in remembering the form of words. On the other hand, oral commands could be carried out from the first; for in all such tests the words were presented to the patient ready formed by the examiner and could be understood without difficulty. Simple printed orders were well executed, but not the complex choice of hand, eye and ear; for this demanded accurate reproduction in sound of the printed symbols.

(2) *Syntactical aphasia.*—Rhythm, verbal balance and grammatical structure are mainly affected in this form of aphasia and, when I first saw No. 13 (cf. p. 401) his speech was jargon. He talked rapidly, but slurred the words and tended to omit articles, conjunctions and prepositions. His pronunciation frequently resembled that of a child who, though fluent, has not learnt to form its phrases. These defects of enunciation and syntax frequently became so gross that it was impossible to understand what he said. If, however, he was made to talk slowly and to break up his answers into short phrases, words emerged used correctly and with a definite meaning; and yet, on a first hearing, he seemed to be talking incomprehensible nonsense.

The rhythmic beat of his phrases and of polysyllabic words was faulty; he could not "touch off" the sounds correctly so as to produce a coherent sequence of properly articulated words or syllables. Simple words and phrases, such as those of the man, cat and dog tests, were repeated after me better than he could say them spontaneously in response to pictures. But with longer and more complex sentences he tended to become confused and to lapse into jargon, even during the act of repetition.

He was perfectly familiar with the names of common objects, and had no difficulty in evoking isolated words; but his mispronunciation of the less usual ones, especially if they formed part of a phrase, rendered them unintelligible without a knowledge of the context. Thus the names he gave to a set of geometrical figures corresponded to their shape, though all but the simplest words were badly pronounced.

He understood what was said to him and chose familiar objects or colours correctly when asked to do so. He even set the clock and carried out the hand, eye and ear tests without fail to oral commands.

He could undoubtedly comprehend the meaning of what he read to himself and executed printed commands perfectly. But it is impossible to reproduce exactly the sounds he emitted, when he attempted to read aloud. Each sentence was said " in one breath "; then after a momentary stoppage he dashed off again. With the original before me I could recognize the words he was saying, but many of them approached so closely to jargon that I should have been unable to do so without this key.

He wrote his name and address correctly, and composed a well-written letter to his mother. Moreover, he put down on paper accurately the names of common objects or colours and the time shown on a clock, omitting the word " minutes." In the same way, when writing from pictures, he left out the conjunctions and the articles and reversed the order, reading from right to left instead of in the normal direction. To dictation he wrote extremely badly, reproducing the same kind of errors that was so evident in speaking. But he copied even long phrases and paragraphs perfectly.

When he said or wrote the alphabet, the order of the letters was defective; but he could read them aloud fairly well and copied them perfectly in cursive handwriting. Obviously it was rhythm rather than form that was most severely affected.

Five years after he was wounded, he had recovered sufficiently to return to his work at an Insurance Office. He was supposed to be normal; but the defects in his use of language, though less severe, were identical in character with those discovered on my first examination. He talked rapidly; single words were well pronounced as a rule, but he occasionally shortened those of more than one syllable. Speech was jerky, because he tended to omit connecting words. Some phrases were run off glibly; others were shortened so as to be said in one breath. When a word was mis-pronounced, he did not go back like a verbal or nominal aphasic, but dashed on in the hope that he would be understood. If checked and asked to repeat what he said, he usually became confused and, the more he was pinned down to making his meaning clear, the worse became his speech. Moreover, his memory for the form of a sentence was defective; if he did not say it at once, he forgot the words of the phrase. He complained, "I say it to myself and it's gone again; don't hold it long enough."

He never used words of wrong significance and the names he gave to familiar objects and to colours were accurate; but those of more than one syllable, such as orange and violet, were badly pronounced.

He understood what was said to him and carried out oral commands perfectly, provided they did not demand the power of recalling some phrase of considerable length. When sent on a message from one department of the office to another, he could perform his task with ease, if he did not think about it; but if, as he went along, he said the message over to himself silently, he could not deliver it clearly and his speech became confused. Owing to insecurity in phrasal formulation and expression, it was difficult for him to go back over the ground freely at will, either aloud or in silent thought, and he avoided every occasion that compelled him to do so.

He carried out all forms of printed command accurately, provided the text remained before him for reference. But, when translating pictures into words, as during the man, cat and dog tests, he still tended to read them from right to left instead of in the normal direction.

He wrote with great rapidity and apparent ease; single words were usually written correctly, but he tended to shorten the phrases and complained, "When find it difficult to pronounce a word, it much harder to write." Writing to dictation was still troublesome to him, although he copied perfectly.

In spite of the comparative ease with which he could now speak, read and write, he still failed to carry out some of the simple tests with the alphabet. He had recovered his power of saying or reading the letters aloud and was able to copy them accurately; but he could not write them down in order or arrange the block-letters in sequence.

He still made mistakes in imitating movements made by me when we sat face to face, or in carrying them out in response to a picture held in his hand. He complained, "Your sitting opposite to me, that helps make the thing a bit mystery. Say to myself, then it's gone again; I lost it, don't hold it long enough." But he found no difficulty in imitating either my actions or those represented pictorially provided they were reflected in a mirror. Asked whether, under such conditions, he said them to himself, he replied "No, simply come automatically; quite simple."

For ordinary purposes this patient was a normal man and had recovered to a great extent his powers of speaking, reading and writing. Yet he still showed a profound disturbance of rhythm and syntax. His capacity to form correct and well balanced phrases was diminished and even single words of more than one syllable were wrongly stressed or shortened. The qualitative aspect of his affection of speech was unchanged and, in spite of the amount to which he had recovered, he still remained a characteristic example of syntactical aphasia.

(3) *Nominal aphasia.*—No. 7 (p. 478) was wounded on October 15, 1917, and, when he came under my care nearly six weeks later, was so grossly aphasic, that it was impossible to obtain from him any coherent information. The few words he uttered were, however, comprehensible, and if he succeeded in producing a short phrase the syntax was perfect and the syllables were touched off correctly. But he could not express himself either in speech or in writing, and had obvious difficulty in discovering a method of formulating his meaning. Throughout, the character of his disabilities remained the same, although he rapidly regained sufficient facility to allow of more extensive observations.

He failed to say his name and address or the days of the week and the months correctly. He could not name familiar objects and colours and was unable to tell the time shown on the face of a clock. His power of repetition was gravely affected, though the sounds he uttered usually bore some remote resemblance to the words said by me.

He showed obvious defects in comprehending the significance of spoken words and phrases. Oral commands were badly executed; he chose common objects or colours after great hesitation, and frequently gave up the attempt altogether. He failed to set the hands of a clock, carried out the coin-bowl test badly, and made many mistakes in the more complex choice between hand, eye and ear. Simpler commands of the same kind were performed with one exception correctly, showing that he still retained some power of appreciating verbal significance.

He had considerable difficulty in understanding the meaning of single words put before him in print and selected familiar objects and colours slowly with obvious effort. He set the clock badly to printed commands, confusing "past" and "to" the hour. In the same way he failed to place the proper coin into the right bowl and made many mistakes with the more complex hand, eye and ear tests. Even simple orders, such as "Shut your eyes," "Put out your tongue" were misunderstood, when given in print.

Shown any two pictures of the man, cat and dog, he found difficulty in evoking the names correctly. If he attempted to read these monosyllabic phrases from print, the results were even worse and he struggled ineffectually to find the correct expressions. Asked to read aloud the orders of the coin-bowl test, he converted them all into numbers and "the second into the third" became "two into three"; but even this simplification did not materially improve his answers.

With great effort he succeeded in writing his name imperfectly, but he could not add his address and failed entirely to compose a letter. He was unable to write down the name of any of the colours shown to him and transcribed the time badly, although he employed numbers only. Writing to dictation was almost impossible; but he was able to copy correctly, using cursive script, interrupted occasionally by irrelevant capitals.

These defects came out clearly when he was tested with the alphabet. Asked to say the letters in order he was unable to go beyond H; he repeated them after me slowly with obvious effort, but read them aloud almost correctly. He was unable to write them spontaneously; had great difficulty when they were dictated, but could copy them in capitals.

He found it almost impossible to state the relative value of any two coins placed before him. Yet in spite of his confused replies, he undoubtedly recognized their monetary value, provided he was not compelled to express the relation of the one to the other in words; for he was able to put together the equivalent of any one of them from amongst a heap of money on the table.

Drawing to order was grossly affected. He drew an elephant without trunk, tusks, eye or ear, and was unable to produce a ground-plan of the ward in which he lay; and yet he could indicate one by one the position of the various objects visible from his bed.

Nearly five years after he was wounded I again had the opportunity of making a further complete series of observations and was able to estimate the extent to which he had recovered. His power to use all forms of language had improved profoundly; but although he could speak, read and write, he remained as definite an example of nominal aphasia as before.

He managed to execute correctly all the serial tasks in which he had failed so lamentably during the six months following his injury. He could name common objects and colours, tell the time precisely, and carry out oral and printed commands. But closer examination showed that any test, which demanded prompt nominal formulation or recognition of differences in meaning between two or more words and phrases, was performed slowly and with some difficulty. An oral or printed order given in a single word was executed quickly; but he hesitated, and was much less certain in his response if it necessitated accurate appreciation of the complex phases of the hand, eye, and ear tests. Above all, however, he found trouble in writing. He could write his name and address and compose a short letter with some effort and expenditure of time; but, when he wrote the name of common objects, the words might be badly spelt, and in his letter to me capitals were interspersed amongst the cursive handwriting in an arbitrary manner. He said: "Well, the . . . the writing or spelling is the worst for me . . . any long words I can't say."

These faults were obvious, when he was tested with the alphabet. Although he was a good scholar before he was wounded, he was still unable to say the letters spontaneously in order, and made similar errors in writing them down on paper. He could write them to dictation and copy them from print; but in both cases he tended to lapse from cursive script into capitals. He even found difficulty in putting together the twenty-six block letters. But he could read and repeat the alphabet perfectly.

His powers of speech were obviously defective to the ear of an observer, and he himself complained that he had difficulty in finding names and that this confused him. He said: "I can say the names . . . unless they might be . . . or . . . big words . . . big names . . . or I can say them all if I have a good look at them . . . read them over . . . have a good look at them and say them over." He did not make repeated attempts to find the right sound of some word he had articulated badly, but paused as if he had been unable to express his meaning. Syntax and grammatical construction were not otherwise affected. These difficulties were equally evident when he attempted to formulate to himself the significance of what he had heard or read.

He had recovered his power to draw an elephant to command, but was still unable to construct a ground-plan of the room in which we worked. If, however, I drew a quadrilateral on paper, and asked him to indicate the position of each object in turn, he did so accurately. He knew where they were, but could not relate them to one another.

He was able to state the relative value of two coins correctly, but added: "It used to be awful . . . I couldn't count the change . . . not correctly . . . it is much better . . . now and again I make mistakes . . . if I try to do it quick, I make mistakes."

This man had recovered to a considerable degree his power of using language and could speak, read and write sufficiently to carry out all the serial tests. But in spite of this profound restoration of function he still remained a characteristic example of nominal aphasia.

(4) *Semantic aphasia.*—No. 8 (cf. p. 415) was wounded on June 4, 1916, and came under my care a month later. At that time he was intelligent, but his memory was extremely poor and he easily became fatigued by any mental effort. He could talk and write, although he complained that he was not able to "reason things out" or keep his mind on what he thought or read.

It was not until seventeen weeks after his injury that I was able to carry out a complete series of tests. Articulated speech was unaffected; the words were well formed and the grammatical structure of the sentences was perfect. He could count and say the alphabet, the days of the week and the months in due order. He repeated them after me exactly, without a mistake. Nothing abnormal could be noticed in ordinary conversation beyond a tendency to become confused and to forget what he wanted to say. He had no difficulty in comprehending the meaning of single words, or even of short phrases, choosing common objects and executing the hand, eye and ear tests correctly to oral commands.

In the same way he understood and carried out a printed order given as a single word or even in a sentence of some complexity. But, when asked to retail the meaning of a paragraph selected from a book or newspaper, he shortened down the contents, saying, "I find difficulty in grasping the general idea of the thing; in reading the newspaper I have to letter out each thing and it does not convey so much to me as it should."

He wrote his name, address and the letters of the alphabet spontaneously and put together a short account of the events of his last

Medical Board, which was coherent and contained no verbal errors. If, however, he attempted to reproduce in writing some passage he had read silently, he eliminated many of the details, complaining that he failed to obtain the "general idea." He wrote easily to dictation, but said, "I can't be sure if I've written it rightly or not."

Thus the crude acts of speaking, reading and writing were not materially affected; he could understand what was said to him and carry out most oral and printed commands. But he was liable to fail in any task which demanded for its performance precise formulation and expression, in words or action, of a general aim and intention. Thus, he had difficulty in reproducing in speech or writing the full significance of a passage he had read to himself; he could remember isolated details, but could not arrange them in order so as to convey their general meaning.

Like all aphasics of this class, the clock tests gave him relatively the greatest trouble; for, although he could tell the time and express it in writing, he was unable to set the hands correctly to oral or printed commands. Moreover, he hesitated and was uncertain, even when setting a clock in direct imitation of one placed before him; he would move one or other hand all round the face to reach a position, which might have been attained by a slight backward displacement. Although in the end his response might be correct, he did not foresee and adopt the easiest method of reaching the goal.

For similar reasons, during the hand, eye and ear tests, he failed even to imitate my reflected movements. Usually this is extremely easy, because the action to be performed by the patient corresponds exactly to that of the observer as seen in the mirror. But, like most semantics, No. 8 tried to reason out what he was required to do and repeatedly came to a false conclusion. He grew confused and sometimes imitated me directly, whilst at other times he reversed his movements, as if we had been sitting face to face. Precisely the same mistakes occurred when he attempted to carry out these acts from pictures reflected in the glass.

Arithmetic gave him considerable trouble and, in spite of his education, he made several mistakes in the simplest addition and subtraction sums.

He had no difficulty in naming any coin shown to him; but, when any two were placed before him, he could not express their relative value with certainty. This led to much confusion in the monetary transactions of daily life.

A simple, straightforward picture was appreciated readily; but, as soon as it conveyed a command, he failed to recognize its full significance. So long as the point of a joke was comprised within the limits of a picture, he could understand it; if, however, for its complete comprehension, he was compelled to combine the picture with a printed legend, he failed to recognize its full meaning.

He had always been extremely fond of drawing and possessed a considerable reputation in his family for his sketches; but since he was wounded this faculty had deserted him. Asked to draw an elephant he moved his pencil aimlessly, saying, "I can't get the idea." Ultimately he succeeded in drawing a figure with an eye, tusks and four legs, but he omitted the trunk.

All sense of direction was lost and, although he could find his way about the house, he complained, "I haven't a clear idea of the whole house, how one room opens into another and that sort of thing."

When at table he found difficulty in picking out the object he required, such as the milk jug. In the same way, during his preparations for shaving, he could not collect the things he required and, when the slides on his belt were displaced, was unable to think how to restore them to their right position.

As might have been expected, all games were impossible and he failed to put together the portions of a puzzle. "I could see the bits," he said, "but I could not see any relation between them; I could not get the general idea."

This patient improved profoundly, and six years after the first examination could carry out all the serial tests without a mistake. But he still showed in a minor degree all those disabilities which had made him so characteristic an example of semantic aphasia; for, although his replies were correct, those actions in which he had failed during the earlier stages were still performed slowly and with hesitation. Thus he could tell the time quickly and write it down with comparative ease, but was less certain when setting the clock to oral or printed commands; it was this group of tests that had given him trouble at first. On the contrary, during the choice of hand, eye and ear, he had no difficulty with orders given by word of mouth or in print, but was slow in imitating movements made by me sitting face to face or shown on a picture held in his hand. For it was in these tests more particularly that he failed during the first five years.

He still showed extraordinary want of power to co-ordinate detail in thought and action; this easily led to confusion and made him appear stupid, in spite of his general intelligence and education. Thus, he wrote down beforehand a series of questions with regard to his future plans, but could not correlate my reply to each one in turn with that to the subsequent question on his list. I was forced to let him ask all his questions seriatim and then to answer the whole of them in a single statement, which he wrote down to dictation. He had regained his power of carrying out simple arithmetical exercises, and on a journey to the East managed his pocket money and kept accounts of his personal expenditure. But he could not estimate the amount of money required for an expedition and was unable to decide on routes or look up the trains ; these he was forced to leave to his companion.

Here again the patient recovered his power of speaking, reading, writing and carrying out all the serial tests ; and yet he still found difficulty in comprehending and retaining the general intention of a task set him, or of formulating to himself the goal of some action he was about to perform.

Chapter III.—The Anatomical Site of the Lesion in some Traumatic Cases of Aphasia.

Such are the views to which I have been led by the study of selected cases of aphasia and kindred disorders of speech. It now remains to discover what relation the site of the lesion, when it can be determined, bears to the clinical manifestations. An ideal example for this purpose would be a chronic aphasic in the prime of life, who, after thorough examination at frequent intervals, had died from some cause unconnected with the central nervous system. One such example came under my notice, but unfortunately an autopsy was refused.

We must therefore be content for the present with the less satisfactory material provided by gunshot wounds and the removal of non-malignant tumours. From an anatomical point of view these injuries are of less localizing value than cases in which a complete microscopical examination could be carried out. But, on the other hand, such patients as I have used in this research are of infinitely greater scientific interest for determining the exact nature of the phenomena during life, than those broken-down wrecks in whom disease was terminated by death. These young men with gunshot wounds of the head were in the prime of youth and their defects of speech and other symptoms were on the mend ; they could be exposed to long continued observations, which would have been impossible in the case of an ordinary aphasic suffering from the diffuse effects of organic disease.

Moreover, in all attempts to associate a lesion of the brain with some form of loss of function, we must always bear in mind the effects of diaschisis. A small area of destruction of tissue can produce profound and widespread defects, if the lesion is acute or progressive. On the other hand a much larger loss of substance may cause a comparatively trivial disturbance, provided it is of old standing, slow onset and has occurred in an otherwise healthy brain.

Many gunshot injuries, which produced clinical manifestations of great interest, were too diffuse to throw any light on the relation between the site of the lesion and the nature of the disturbance of speech. But amongst my cases were a small number which seemed to bear on this question and these I shall consider in closer detail in the following pages.

§ 1.—*Methods employed for determining the Position of the Cerebral Injury.*

In every instance of an injury to the head which came under my care during the war, the relative extent and shape of the wound were recorded on a set of diagrams showing the head from different aspects. An X-ray photograph was taken from the front and from the side and in many cases stereoscopically, especially where we desired to localize the position of some foreign body in the substance of the brain.

Measurements were made according to the following plan. The distance from the root of the nose to the external occipital protuberance along the middle of the scalp was recorded in centimetres and the point determined at which it was cut by the interaural line. Then the position of the wound was mapped out, its diameters measured and the distance of its various parts determined in relation to the nasion-inion line and the middle of the scalp.

After the wound had healed, the head was subjected to another complete examination, to determine the extent to which bone had been lost and the condition of the parts that covered the opening in the skull.

If an operation was performed, I was invariably present to record its nature, the parts removed and any indications that could be used for cerebral localization. Such autopsies in the living often furnish evidence of the greatest value.

In order to determine the exact site of these brain injuries, I attempted to reconstruct them on the cadaver. For this purpose I applied for help to Professor Elliot Smith, who not only placed all the resources of his Anatomical Institute at my disposal, but poured out for me his unique knowledge and experience of cerebral topography. I cannot sufficiently thank him and his assistants, Dr. Shellshear, Dr. John Hunter and Dr. Tudor Jones for the enthusiastic manner in which they helped and guided me in my difficult and laborious task.

The method we adopted was as follows. The head of a male body was selected, which corresponded as nearly as possible in its measurements to that of the patient, whose wound we intended to localize. The exact extent of the loss of bone was marked out on the scalp and holes were drilled through the skull to mark its dimensions. Through these a coloured fluid was passed with a small brush to fix the relation of the bony opening to the surface of the brain. Then the skull-cap was removed and a cast taken of its inner surface. This gave us a solid reproduction of the brain, covered by its membranes, on which were indicated the limits of the external wound. The situation and course of the principal fissures were determined by careful dissection and drawn on the cast. Thus we finally obtained a record of the area occupied by the wound on the surface of the brain, together with its extent in relation to the main landmarks of cerebral topography.

Fortunately the size of the head in these patients fell into a comparatively small number of groups; by selecting cases where the wounds were far apart, and by employing both halves of the brain in each cadaver, we were able to reduce the expenditure of bodies within reasonable limits. But none the less I cannot sufficiently express my thanks to Professor Elliot Smith for his open-handed generosity.

§ 2.—*The Site of the Lesion in various Forms of Aphasia due to Gunshot Injuries of the Skull.*

(*a*) *Verbal Defects.*

No. 6[1] (see fig. 1) formed an excellent case for our methods of anatomical localization. For the wound was an almost vertical cut in the left temporal region, 5 cm. in length, penetrating all the tissues, including the bone. The dura mater was laid bare in its deepest part, but the brain substance was not exposed. There was no widespread fracture of the skull and healing was complete in thirty days. No operation was performed at any time.

The upper end of this linear incision was 5·5 cm. from the middle of the scalp and 14 cm. behind the root of the nose; it lay 0·5 cm.

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[1] Fully reported in the Appendix, p. 447.

anterior to the interaural line, whilst its extreme lowest point was 3 cm. in front. The whole nasion-inion measurement was 34·5 cm. and this was intersected at 14·5 cm. by the interaural line.

When this wound was plotted on the brain of a skull with approximately the same measurements, it was found to lie over the anterior portion of the precentral gyrus, extending downwards onto the inferior frontal convolution.

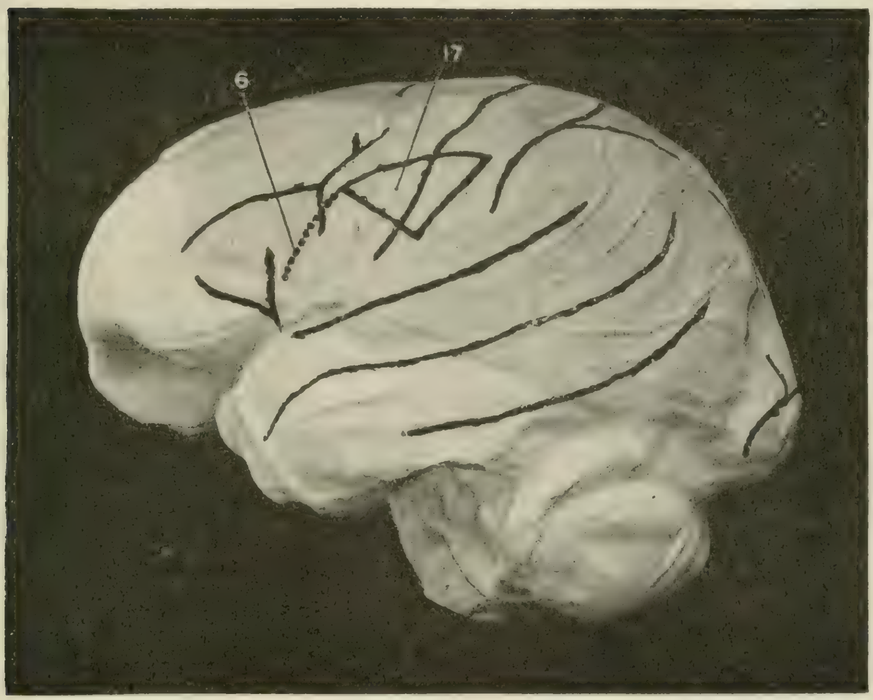

FIG. 1.

On admission to the London Hospital four days after he was wounded, this patient was speechless, but he soon began to make articulate noises, which seemed at first to bear no relation to the words he was striving to pronounce. He could neither say his name spontaneously nor repeat it after me. His power of finding words rapidly improved during the first month, although throughout it was verbal structure and not nomenclature that formed his main difficulty.

He could understand what was said to him, and commands exacting a single choice were carried out accurately, but, as soon as two of these orders were combined, his response became slow and hesitating.

Comprehension of printed phrases was obviously defective. He wrote his name and address correctly, but not that of his mother with whom he lived. When he attempted to record the names of objects he saw from the window, the words showed the same kind of structural faults as his articulation. Simple phrases were badly written to dictation, but he could transcribe print into cursive handwriting. He counted with extreme difficulty, although he wrote the numbers up to 21 correctly.

When examined more closely, five months after the injury, he still had great difficulty in verbalization. The words were badly formed and expressed with difficulty, although they corresponded in nominal significance to what he wanted to say. He did not employ wrong words and his power of naming was perfectly preserved.

He understood what was said to him and carried out oral commands slowly, but on the whole correctly.

His power of comprehending the meaning of what he read to himself was undoubtedly good, and he carried out printed commands with several corrections, though few actual errors. As soon as he was permitted to read them aloud, his responses became perfect, for the sound of the words formed a self-given oral command.

Associated with these disorders of verbal formulation and expression he showed no abnormal physical signs in the nervous system, except a transitory weakness of the right half of the lower portion of the face and some deviation of the tongue to the right. All the reflexes, including the abdominals and plantars, were normal; there was no affection of motion, no incoordination, no disorder of sensation, and the visual fields were not diminished.

This man formed a splendid example of what would have been called true "motor" aphasia. Evidently, however, he suffered from more than an "anarthria," even in the highest significance of the term, for his powers of internal verbalization were affected, as shown by his difficulty in writing and faults of spelling. But he still retained his power of naming correctly, provided he was able to utter a sound which corresponded sufficiently to the name he was seeking.

No. 17 (see fig. 1) was much less satisfactory from the point of view of anatomical localization; for the extraction of a rifle bullet from the substance of the brain was followed by formation of an abscess, which undoubtedly caused a considerable amount of deep destruction. But he was a superb example of defective verbal formation and, as a student of medicine, was able to give valuable introspective information with regard to his symptoms.

About ten days after he was wounded he was trephined in France, and a rifle bullet was removed from the brain in the " left Rolandic region." When he came under my care five months later, the wound was represented by a sinus from which issued a considerable quantity of pus. This opening was situated 16 cm. backwards along the nasion-inion line, in the centre of an irregular area, from which bone had been removed; this measured 4·5 cm. vertically, and 6 cm. horizontally, and extended between two points 13 cm. to 19 cm. posterior to the root of the nose. The upper border of the bony opening lay 6 cm. from the middle line of the scalp.

After removal of some fragments of bone from the substance of the brain and efficient drainage of an abscess cavity, the wound finally healed within eight months from the injury.

When the extent of this bony opening, which corresponded to those parts denuded of dura mater, was plotted on the surface of the brain, it was found to occupy an area extending between the inferior precentral and the lower third of the post-central fissures (fig. 1). It corresponded in front with the upper part of the incision in No. 6, but did not extend so low. On the other hand, the destruction was not only superficial, but extended deeply into subcortical regions of the brain.

He showed characteristic difficulty in finding words to express his thoughts, and said, " At first I don't think I had more than a twenty-word vocabulary." Words were uttered singly or in short groups, isolated by pauses of varying length, and a single word of many syllables was liable to be slurred. Even a year after the injury he could not say the alphabet perfectly, and had much difficulty in counting. He was able to repeat the content of what was said to him correctly, but had the same difficulty in word formation as during spontaneons speech.

He seemed to understand completely what he heard, and oral commands were executed quickly and with accuracy. But he confessed that, for the first fortnight after he was wounded, he had difficulty in understanding things said to him, unless they were " very simple and said very slow."

He carried out printed commands correctly, but could not read to himself with comfort, nor could he be certain that in the long run he understood exactly what was in the book before him. " I can get the meaning of a sentence, if it's an isolated sentence, but I can't get all the words." When he read aloud, his articulation showed the faults evident during voluntary speech, though to a less degree.

He wrote slowly and with great effort; his spelling was preposterous considering his education, and the form of the words showed the same defects that were manifested in voluntary speech. He complained, "I have to spell out every word, even the little ones; I have to say 'of'—I know it's a preposition, but then I have to think is it 'to' or 'from' or 'of.'" So much was this a matter of defective verbal formulation, that in writing a simple word like "help" he found it difficult to remember if the l or the p came last. A word such as "manager" was spelt "man-ger" exactly as it was pronounced, even when writing silently.

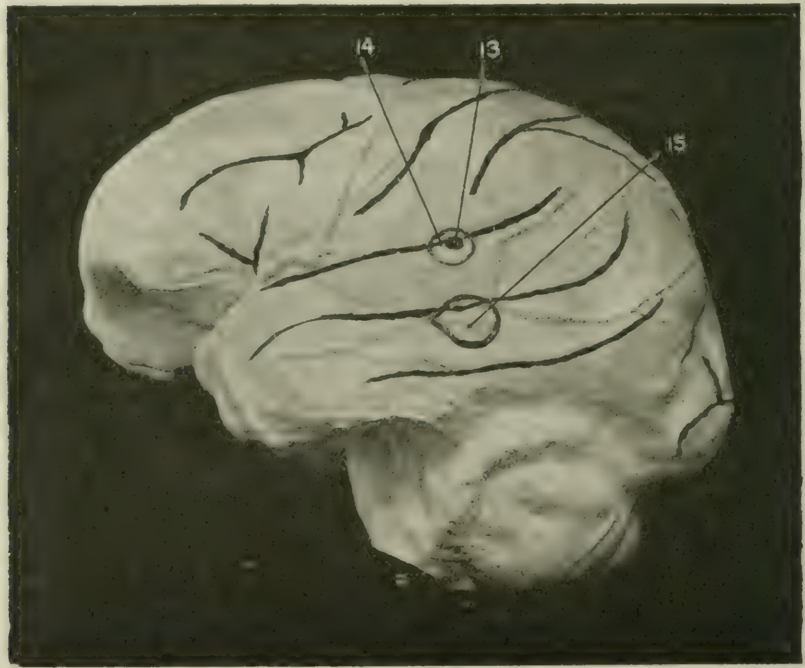

FIG. 2.

He showed remarkable powers of arithmetic and checked his own bank-book, in spite of his difficulty in counting. When he uttered a wrong number, as for instance whilst scoring at bridge, or looking up the page in a reference book, the false number did not mislead him; if he said twenty-eight instead of forty-one he scored it as forty-one. "I do the sum right, but get the figures wrong."

As might have been expected from the nature of the lesion, these defects of speech were accompanied by signs of profound injury to the nervous system. For a time he suffered with Jacksonian convulsions, which began in the right hand; these, however, passed off gradually, but were always accompanied by some increased loss of verbal capacity. He showed the characteristic signs of a spastic hemiplegia; isolated movements of the right hand were impossible, and although he possessed considerable power at the elbow and shoulder, the movements were clumsy and the whole limb was hypertonic. The right leg was in a state of extensor rigidity accompanied by loss of power of dorsiflexion at the ankle. The lower portion of the right half of the face was somewhat affected and the tongue was protruded to this side of the middle line. Gross sensory changes of the cerebral type were present in both arm and leg of the affected half of the body. All the deep reflexes were greatly exaggerated on the hemiplegic side, the plantars gave a characteristic upward response and the abdominals were absent. Vision was unaffected and the fields were of normal extent.

This is another excellent example of so-called "motor" aphasia. He recovered to such an extent that the last traces of his disorder of speech were manifested solely as slight defects of word-formation. But these were evident not only on articulation and in his writing, but also when he attempted to formulate a word to himself for the use of internal speech. The power of naming was unaffected throughout, from the moment when it could be definitely tested.

(*b*) *Syntactical Defects.*

Pick [11] has always contended that "agrammatism," as he defined it, was produced by lesions of the temporal lobe; and, in so far as it is included under "syntactical defects," my experience exactly bears out his contention. It is important, however, to remember that not all forms of jargon belong to this group of disorders of speech.

No. 15[1] (see figs. 2 and 3) was a typical example of this condition. A rifle bullet had entered just to the left of the inner canthus of the right eye, destroyed the left eye, and had made its exit directly above the insertion of the left ear. A month later the wound of entry was represented by a minute perfectly healed white scar. On the other hand, the exit consisted of an irregular opening in the bone and tissues of the scalp, through which protruded a small pulsating hernia cerebri. Bone had been removed over an irregularly quadrilateral area about 3 cm. in vertical and horizontal extent; below, this opening reached the level of the insertion of the ear and above it was about 13 cm. from the middle line of the scalp, corresponding anteriorly to a point on the nasion-inion line 13 cm. from the root of the nose. The total distance from the nasion to the external occipital protuberance was 35 cm.

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[1] Reported in full in the Appendix, p. 459.

Thus, the track of the bullet passed back through the left temporal lobe, entering its substance in front close to the tip and passing out at the level of the insertion of the left ear (fig. 3). When plotted on the surface of the brain, the exit wound lay over the middle of the second

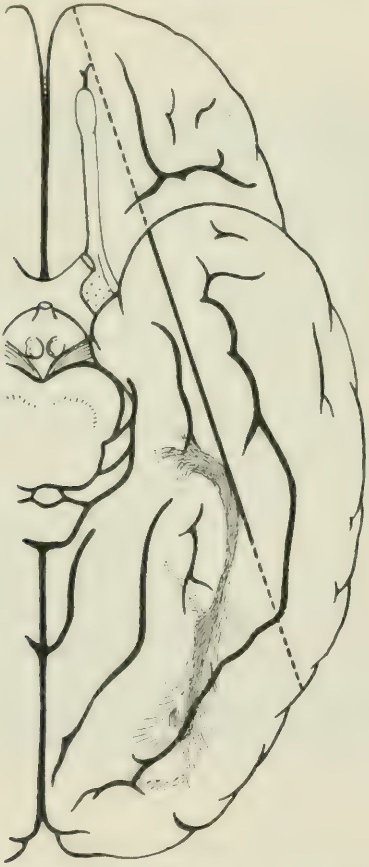

FIG. 3.—To show the course of the bullet in No. 15.

temporal convolution, but must have produced some destruction both above and below the superior temporal fissure (fig. 2). In its course it injured the extreme lower fibres of the optic radiations and so produced the upper quadrantic hemianopia described by Cushing [5] as characteristic of lesions within the temporal lobe. This wound healed completely in eighteen weeks.

His speech was a perfect example of that form of jargon which is due to disturbance of rhythm and defective syntax. He did not use wrong words and, if the subject under discussion was known, it was not difficult to gather the sense of what he said. Once started, his speech was rapid and he tried to "rush" his phrases until he was arrested by the utterance of pure jargon. It was extremely difficult to hear the prepositions, conjunctions or articles, and these parts of speech were frequently omitted. The same errors marred his attempts to read aloud; even when reading to himself, he became confused by internal jargon and lost the significance of all but the simplest phrases. His spontaneous writing was poor and he had little power of reproducing in written words the contents of a paragraph he had apparently read with understanding. His defective power of orderly symbolic formulation and expression led to a curious error when he was asked to draw an elephant; he said "irons," "highons" for tusks, and so provided the figure with horns, although he was able to correct his mistake by suitable gestures. His power of naming was preserved, although his nomenclature was sometimes unusual and he could tell the time correctly. On the whole he understood what was said to him, unless he was compelled to repeat it to himself. Simple oral commands were well executed, but he hesitated and made several errors over the complex hand, eye and ear tests.

On his admission to the London Hospital, a fortnight after he was wounded, there was a little weakness of the lower portion of the right half of the face and the tongue deviated slightly to the right. There was no loss of motion or sensation in body or limbs. The deep reflexes were somewhat greater on the right than on the left side; the right plantar reflex gave an upward response and that from the half of the abdomen was diminished. All these abnormal signs passed away entirely within five months from the date of the wound, leaving only the upper quadrantic hemianopia, as far as such a condition could be observed in the one remaining eye.

This was a perfect case for our methods of localization. Beyond a transitory affection of the reflexes and slight defect in the movements of face and tongue, there was nothing to point to any morbid condition beyond the limits of the temporal lobe. Moreover, the form of the visual field, as far as it could be determined from the one remaining eye, together with the curious attacks of "smells" accompanied by "dizziness," were characteristic of a lesion in this part of the brain.

Number 13 (fig. 2) would have been equally valuable from the point of view of localization, had it not been for the uncertainty introduced by the operation, carried out at the Front.

He was struck by a shell-fragment in the left temporal region, but did not become unconscious. When he came under my care about three weeks later, he brought no records of any kind. It was obvious that some operation had been performed; for there was a long, linear, surgical scar extending from the fronto-temporal to the parietal region on the left side of the head. This incision had closed, except for a small granulatory area in front, which healed rapidly and was of no importance. Farther back was a pouting sinus, which exuded pus; it was level with a point 16 cm. along the nasion-inion line and lay 8 to 9 cm. from the middle of the scalp. An X-ray photograph showed that bone had been removed over an irregular oval area, which lay exactly under this suppurating opening and was bisected by the surgical incision. On plotting out this area on the surface of the brain it was found to lie just behind the central (Rolandic) fissure.

But exactly below this area, 11 cm. to the left of the middle line, lay another fungating sinus passing down to and apparently penetrating the bone, from which exuded a considerable quantity of pus. The skull had not been trephined in this region, and yet the probe passed through an opening into the cranial cavity. Moreover, the orifice in the scalp was at a distance from the surgical incision and had not been subjected to operative treatment of any kind. It undoubtedly represented one of the original wounds and, when plotted on the surface of the brain, lay over the upper portion of the first temporal gyrus and the Sylvian fissure, on a level vertically with the foot of the post-central fissure (fig. 2).

I should like to suggest that this was the lesion responsible for his loss of speech. The patient on receipt of the wound was obviously aphasic and the missile had possibly injured the skull in the neighbourhood of the Rolandic region. The surgeon therefore performed a linear exposure and trephined over the central fissure: but he paid no attention to the small wound at a lower level over the temporal lobe, which had also perforated the skull.

Both openings healed completely within eight weeks from the date of his wound.

The disturbance of speech produced by this injury has already been summarized on p. 383; it formed a beautiful example of syntactical defects of symbolic formulation and expression. The rhythm of speech was disturbed and syntax was defective, whether the words were spoken or written. Naming, and comprehension of oral or printed commands were perfect. The character of these disorders in the use of language remained essentially unchanged five years after he was wounded, in spite of profound improvement in his power of speaking, reading and writing.

Associated with these defects of speech, he showed very few abnormal physical signs of cerebral injury. He had no fits or seizures of any kind. Vision was unaffected and the fields were of normal extent. At first the movements of the right angle of the mouth were slightly less than those of the other side, and the tongue was protruded a little to the right; but this passed away quickly. He complained that the right hand "felt different"; the grasp was comparatively feeble, but individual movements of the fingers were possible and they were somewhat hypotonic. There was distinct ataxy of the fingers with the eyes closed, and the power of recognizing passive movement and posture was defective in the right hand. Form and weight were correctly appreciated and localization was perfect. The lower extremity was unaffected. All the reflexes, including the plantars and abdominals, were normal.

The lesion responsible for these changes lay over the middle of the first temporal gyrus; but the slight disturbance of the higher aspects of sensation in the right hand during the earlier stages pointed to some affection of the post-central convolution.

No. 14 (fig. 2) suffered from a much more severe injury, which lay, however, exactly over the same situation as what I have presumed to be the effective wound in No. 13.

He was hit by a fragment of shell casing or by shrapnel just above the insertion of the left ear. When I first saw him seventeen days later, the wound was represented by a granulating surface of 2 cm. by 1·5 cm. situated 11 cm. from the middle of the scalp and 16 cm. backwards along the nasion-inion line. This unhealed patch was surrounded on three sides by a horse-shoe shaped incision, which had united firmly. Within lay an irregularly quadrilateral area, where the bone had been removed; this was covered by normal scalp except over the site of the original wound.

When this was plotted on the surface of the brain, it was found to occupy the first temporal gyrus and the Sylvian fissure exactly as in No. 13 (fig. 2). But the trephined area was more extensive, especially in front and above, and there can be no doubt that it extended forwards to the lower portion of the central fissure.

At first he was too ill for complete examination, but his speech was the most extraordinary jargon. There could be little doubt that he knew what he wanted to say, although the words poured out in phrases which had no grammatical structure and were in most cases incomprehensible. In many instances the words themselves were well formed, but they had no meaning as they were uttered; occasionally, however, sufficient words were correctly placed to make his meaning clear. He could not repeat a sentence said to him and, when he attempted to read, uttered pure jargon.

He was unable to find names for common objects of daily use and yet his correct choice to printed command showed that he was familiar with their usual nomenclature.

Comprehension of spoken words was obviously defective and he was liable to be puzzled by any but the simplest oral commands. Time after time, in general conversation, he failed to understand what was said and to carry on a subject started by himself. Spontaneous thought was rapid and correct and his intelligence of an extremely high order, but his power of symbolic formulation and expression was hampered by the defects of his internal speech.

He undoubtedly comprehended what he read in the newspaper and demonstrated to us the movements at the Front on large-scale military maps. He understood French and amused himself with a work on Napoleon's Russian campaign. But any attempt to reproduce aloud what he had read resulted in incomprehensible jargon. Asked to read aloud the commands of the hand, eye and ear test, he could not do so, although the movements were executed perfectly and without hesitation.

Single words were, for the most part, so much more easily written than spoken, that he carried about paper and a pencil to help him out of his conversational difficulties. When at a loss, he would write something sufficient to convey his meaning to his puzzled auditor. But he was unable to read what he had written and this, together with his difficulty in forming phrases and sentences, made it impossible to compose a letter or coherent account of something he wished to convey. He could copy perfectly, but wrote badly to dictation, because of the rapidity with which he forgot the phrase that had been said to him.

He could play the piano, read the notes correctly and evidently recognized the constitution of a chord and the changes of key.

These characteristic defects of speech were associated with extensive signs of cerebral injury. He developed seizures in which he ceased to talk and the right arm fell powerless on to the bed. He was never convulsed and did not appear to become unconscious in all these attacks, although he was ultimately found dead in his bath; but he was unable to speak and found he was powerless to think. These attacks were preceded by a "hot" or "tingling" feeling down the right arm and leg, accompanied by a taste and smell and a peculiar state of mind, which he could not describe in comprehensible terms.

Even when I saw him first, he did not suffer from headache and vomiting. The optic discs were normal and there was no hemianopia. Movements of the lower part of the right half of the face were defective and the tongue deviated to this side. The deep reflexes on the right half of the body were brisker than those on the left and the plantar gave an upward response; the superficial reflexes from the right half of the abdomen were greatly diminished compared with those of the left. These abnormal signs passed away entirely in about a year from the time he was wounded.

In spite of the difficulty he found in executing movements to command, I was able to show, even in the early stages, that there was no absolute paralysis of the right upper or lower extremity; isolated movements of the fingers were possible, but there was extreme inco-ordination of both arm and leg. Subsequent examination confirmed the original supposition, that his loss of power was mainly afferent in origin.

In consequence of a lesion, which fell mainly over the middle of the first temporal gyrus, this patient suffered from profound syntactical defects of symbolic formulation and expression. His speech, both external and internal, was jargon and he could not write coherently. But the injury produced more severe general effects than those of No 13. For he not only suffered from seizures, with a characteristic aura of smell and taste accompanied by a dreamy mental state, but also showed in the earlier stages profound inco-ordination and signs of afferent disturbance in the right arm and leg.

(c) *Nominal defects.*

No. 7[1] was wounded by a fragment of a high-explosive shell, which produced a compound depressed fracture of the skull in the left parietal region, with laceration of the dura mater and protrusion of brain substance. He came under my care, nearly six weeks later, with a

[1] Reported in full in the Appendix, p. 478.

granulating stellate wound, which destroyed all the structures down to the brain. In front it was 7 cm., behind 9 cm. from the middle of the scalp and it extended between two points 19·5 cm. and 27 cm. on the nasion-inion line. An X-ray photograph showed an area of removal of bone in the anterior parietal region, measuring 4 cm. by 2 cm. at its broadest part, with a fissured fracture running directly forwards. The wound healed finally eight weeks after it was inflicted.

While this injury was plotted on the surface of the brain (figs. 4 and 5) it was found to occupy an area shaped like an arrow-head, pointing upwards and forwards within the limits of the angular gyrus (area angularis of Brodmann [1]).

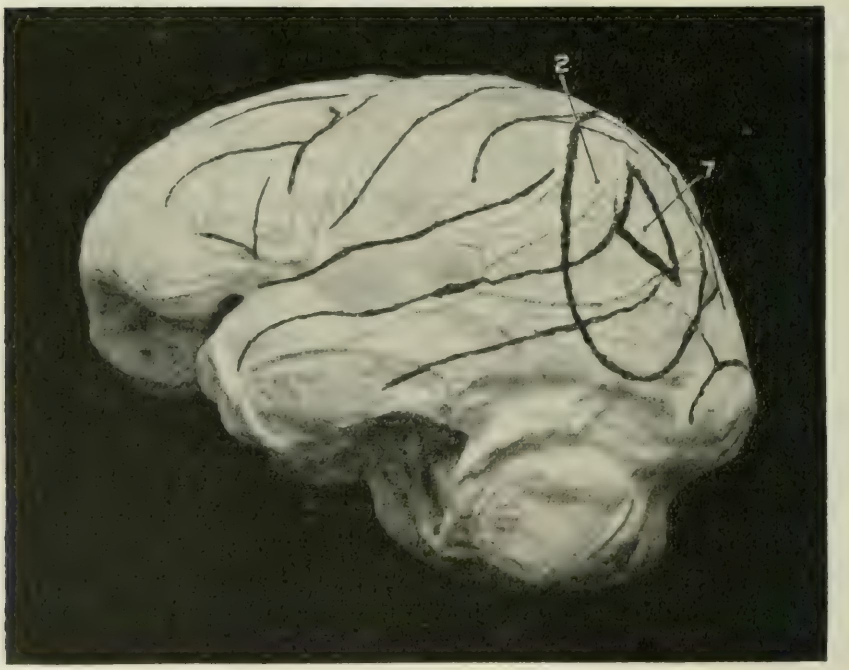

FIG. 4.

On admission to the London Hospital nearly six weeks after he was wounded, he was so grossly aphasic that no coherent information could be obtained from him. The words he uttered were comprehensible, but he could not find means to express himself in speech or writing. On p. 386 I have summarized his condition at various periods after he was wounded. Throughout, the character of his disabilities remained the same, although he rapidly regained sufficient facility in utterance for daily intercourse; even five years and nine months after the injury his speech was demonstrably abnormal and he was still an excellent example of nominal aphasia.

Fortunately in this case there were no signs pointing to gross injury of the deeper structures of the brain. He suffered from no convulsions or seizures. Vision was in every way normal. Movements of the face and tongue were unaffected and he showed no changes either in motion or sensation. The reflexes, including the abdominals and plantars, were equal on the two sides.

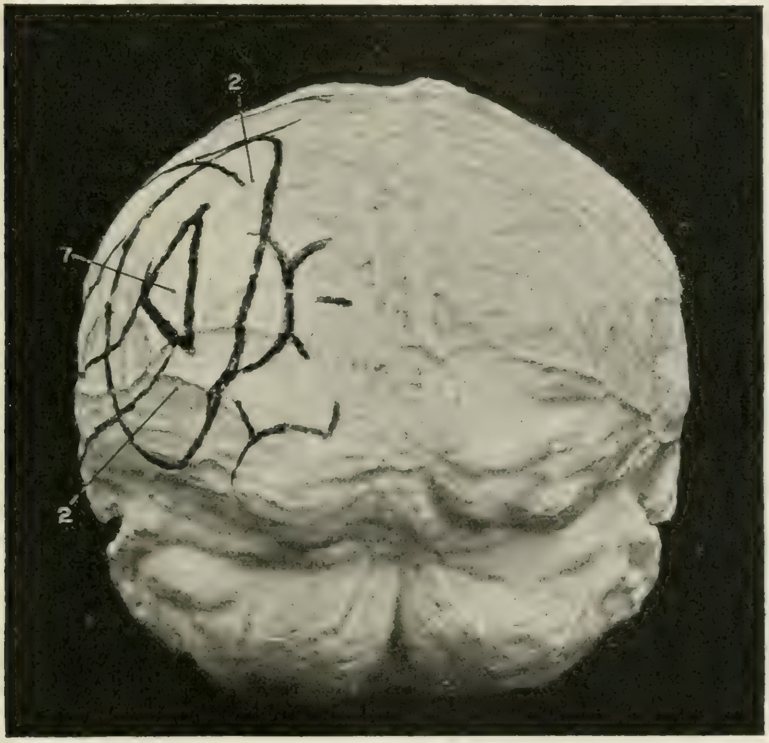

Fig. 5.

This man formed a superb example of the condition I have called nominal aphasia, in which the principal defect consisted in want of power to name objects and to recognize exactly the meaning of words presented orally or in print. The lesion lay over the angular gyrus and was comparatively superficial.

No. 2 (figs. 4 and 5) was of much less value for purposes of anatomical localization. The lesion was extensive and deep, at any rate in the centre; but the clinical observations were of unusual completeness and interest owing to the great intelligence of the patient, and to my repeated opportunities for examining him over a period of more than four years.

This young Staff-officer received a compound fracture of the skull in the left parieto-occipital region from the kick of a horse. Fragments of depressed bone were removed by operation, carried out within a few hours of the accident, and the brain below the injury was found to be reduced to pulp for a depth of about three inches (about 7 cm.). Right hemianopia and "some degree of aphasia" were present from the first, but motion and sensation were never affected.

When he first came under my care some six months afterwards, the wound was firmly healed, and lay within a depressed oval area, where the skull had been removed. At a subsequent operation we were able to measure the exact limits of this opening; its largest diameter, pointing upwards and a little forward, was 10 cm., while horizontally it measured 5·5 cm. at its broadest part. Looked at from behind, its superior border was opposite a point 23 cm. along the nasion-inion and 3·5 c.m. to the left of the middle of the scalp; below it reached a point 33 cm. on the nasion-inion line and 3·5 cm. to the left.

During the operation to repair this opening, Mr. Trotter cut a piece of rubber of the exact size and shape to act as a guide. This was subsequently of great help in plotting out the site and extent of the injury, for we were able to fix this oval patch on to the skull of the cadaver and drill through to the brain to mark its boundaries. (Figs. 4 and 5.)

In this way we found that the area of loss of bone occupied the angular, superior parietal and parieto-occipital gyri; its anterior border extended as far forward as the middle of the supra-marginal. But we must bear in mind that this gives the extreme limits of the injury, within which the destruction of brain tissue occupied an unknown but smaller extent.

This patient suffered from profound loss of power to name common objects or colours, and to use nominal expressions in ordinary conversation. Most of the words at his disposal were well pronounced and intonation was normal, but, when he had difficulty in finding a name, he would try various combinations of sound more or less related to the word he was seeking. He was able to give long explanations of his inability to find the right names, and could use appropriate metaphorical expressions to designate colours that he could not name. If he failed to find a word, he could repeat it accurately after it had been said to him.

He showed obvious difficulty in grasping the exact meaning of what was said, especially such words as "up" and "down," "back" and "front," "to" and "past" the hour, when contrasted with one another. He could choose familiar objects slowly but correctly to oral command; with colours, he hesitated greatly and made several mistakes. He could not set the hands of the clock or carry out the complex hand, eye and ear tests to orders given by word of mouth.

He was unable to read a newspaper to himself or to comprehend exactly the meaning of a printed paragraph. Common objects were chosen slowly but correctly to printed command, although he hesitated greatly with colours. If the order to set the clock was given in printed words, it was badly executed; but he had no difficulty when they were replaced by numbers. The hand, eye and ear tests were performed extremely badly if he read the words silently; when, however, he read them aloud the orders were executed without fail.

He wrote his signature, but could not add his address, and was incapable of writing a letter or giving a written account of what he had heard, seen or read. Later, he regained this power somewhat, although his spelling was so incredibly bad that many of the words were scarcely recognizable. Writing to dictation was faulty, and he copied printed letters accurately in capitals, but could not transcribe them with certainty into ordinary handwriting.

He could count aloud, but wrote the names of the numbers extremely badly. He was unable to carry out even simple arithmetical operations and had difficulty in expressing the relative value of two coins, although he was evidently conscious of their fundamental relation,

He could make an excellent drawing from a model and reproduce it later from memory; but his drawing of an elephant to command was absurd, though, when trying to explain the difficulties of transport in Mesopotamia, he produced spontaneously a spirited sketch of a camel.

He was unable to draw a ground-plan, in spite of the fact that he possessed strong visual images and orientation was not fundamentally affected.

He suffered from no fits or seizures at any time. There was complete right hemianopia to movement, form and colour, which remained unaltered throughout; apart from this, vision was normal. Otherwise there were no abnormal signs of any kind in the central nervous system.

This is a splendid example of what I have called "nominal" aphasia in a man of unusual intelligence and education. The power of naming and appreciating verbal meaning was defective, although he retained the capacity to formulate the end and aim of a symbolic act. We do not know exactly the situation of the brain lesion, but it must have lain within limits which comprised mainly the angular, superior parietal and parieto-occipital gyri. It thus includes the whole of the more localized lesion found in No. 7.

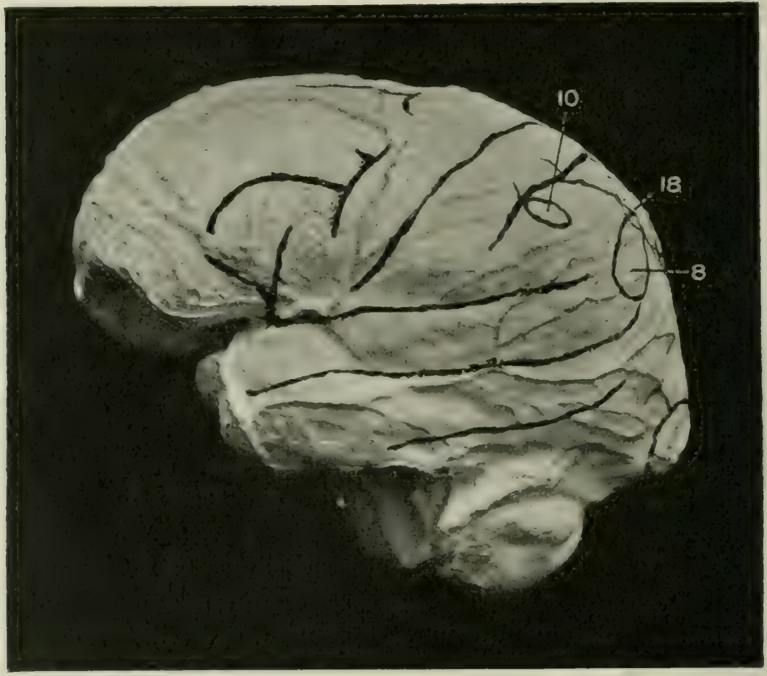

Fig. 6.

(*d*) *Semantic Defects.*

No. 10[1] was wounded accidentally over a small area in the left parietal region by the premature explosion of a hand-grenade. At the operation next day the dura mater was found to have been perforated in two places and two small fragments of bone were removed from the brain.

When he came under my care, thirty-four days later, the wound had healed completely. Bone had been removed over an oval area 2·5 cm. by 1·25 cm., extending between two points 15·5 cm. and 18 cm.

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[1] Reported in full in the Appendix, p. 498.

along the nasion-inion line at a distance of 8 cm. from the middle of the scalp.

On plotting the site of this lesion, it was found to occupy the anterior portion of the supramarginal gyrus, bounded in front by the post-central fissure (figs. 6 and 7). It was of small size (less than 2·5 cm. by 1·25 cm.) and did not extend deeply into the substance of the brain; this was confirmed at an exploratory operation carried out whilst he was under my care.

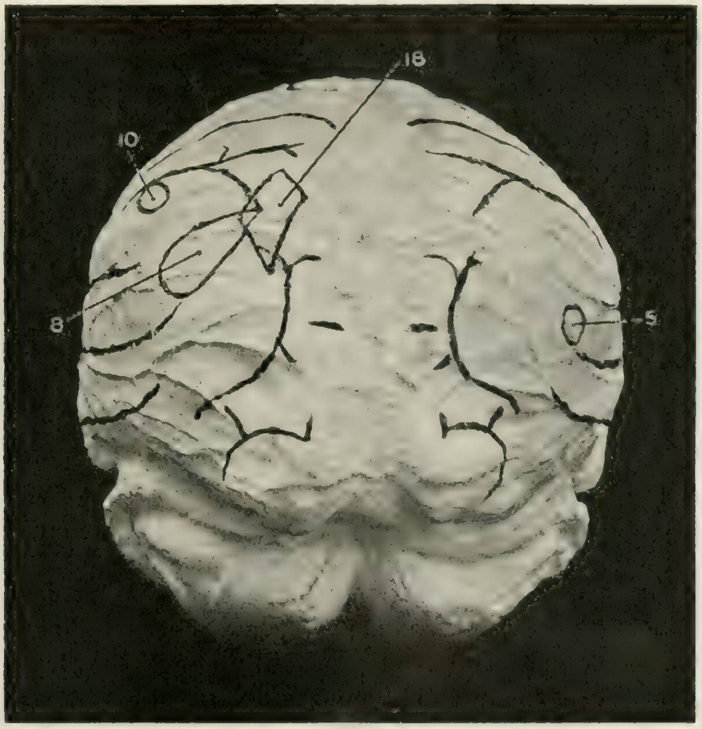

FIG. 7.

This patient was a splendid example of what I have called semantic defects of speech. He could name objects or colours shown to him and had no difficulty in finding or articulating words to express his ordinary needs; his phrases were perfectly formed and spaced. But in general conversation he paused like a man confused, who had lost the thread of what he wanted to say. Words and phrases said to him were repeated correctly, provided they did not contain a number of possible alternatives.

He chose an object or colour named by me, but had obvious difficulty in setting the clock or carrying out the hand, eye and ear tests to oral commands. He was easily puzzled and became confused as to the aim of the task set him.

He understood the significance of printed words and short sentences provided they did not contain a command. But he gave a poor account of the general meaning of a series of short paragraphs he had read silently to himself; his narrative tailed away aimlessly, as if he had forgotten the goal for which he was making.

He read aloud simple sentences without mistakes, but tended to doubt the accuracy of the words he had uttered correctly.

His handwriting was profoundly altered; he wrote with extreme rapidity, as if afraid of forgetting what he wanted to transfer to paper, and he tended to employ the same symbol for d, f, o, r, t, and v. Apart from the bad writing and the use of this peculiar letter, he copied correctly; he showed the same defects to dictation and, in addition, he repeatedly forgot what he had been told to write.

Although he counted excellently, he was unable to carry out the simplest arithmetical operation; and this was the more remarkable as he had been an accountant, accustomed to handle complex masses of figures. He was confused by the relative value of coins and had much difficulty in ordinary life with change and the price of his purchases.

He could not draw from the model or from memory, and was completely unable to delineate an elephant to command. He failed entirely to draw a ground-plan of a familiar room and was unable to express the relative position of its salient parts or the objects it contained.

Orientation was gravely affected; he was liable to lose his way in the street or hospital, and had difficulty even in finding his own room.

He could play no games and "puzzles" worried him greatly.

These defects of symbolic formulation and expression were associated with no other signs of structural disorganization. Vision was perfect and the fields were of normal extent. Face and tongue moved well and equally. There was no paralysis of motion; sensation was unaffected, even to the most delicate tests. The reflexes, including the abdominals and plantars, were equal on the two halves of the body.

In this case the sole disturbance produced by a lesion in the supramarginal gyrus was inability to comprehend and to maintain in consciousness the general significance of some symbolic representation, or the intention of an act he was about to perform, either to command or on his own initiative.

No. 5 (figs. 8 and 7) was the only left-handed man in my series, and the wound, due to a rifle bullet, was situated in the right parietal region. On admission to the Base Hospital, this was a minute punctured opening, from which exuded cerebrospinal fluid mingled with small quantities of disintegrated brain matter. The bullet had bored a circular hole in the skull, perforated the dura mater, and was extracted from a point in the brain about 4 to 5 cm. in depth.

When he was admitted to the London Hospital a fortnight later, the wound of entry was healed and covered by a minute scab, situated 20·5 cm. backwards along the nasion-inion line and 11 cm. from the middle of the scalp. The semicircular surgical incision had healed by first intention.

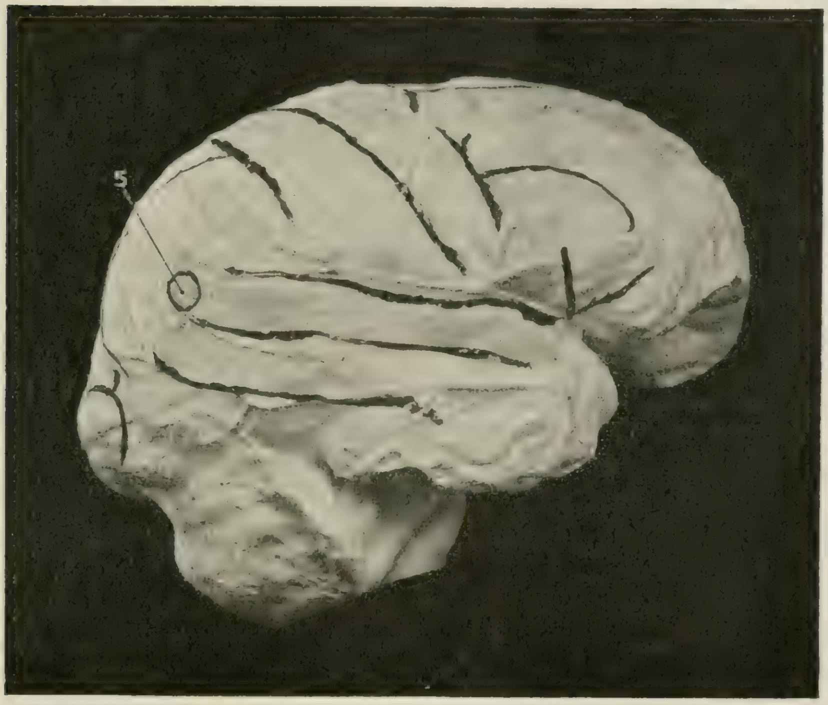

Fig. 8.

On plotting the position at which the bullet had entered the brain, it was found to lie over the inferior and posterior portion of the supramarginal gyrus (figs. 8 and 7). The removal of the bullet, lying some 5 cm. deep in the brain, undoubtedly produced more destruction of substance than in the case of No. 10.

Here again the most striking feature was his inability to formulate to recognize and to retain in his mind the exact general intention of some action requiring symbolic representation.

Articulation was perfect, words were produced without difficulty and the rhythm of the phrase was unaffected. His sole defect was shown in a tendency to forget the exact general intention of what he wanted to express; sentences died away without reaching their formal conclusion. He could name common objects or colours correctly, and repeat single words or even sentences, provided they did not comprise many independent statements. The first few phrases of a long paragraph might be repeated correctly, but as the test proceeded he would lose touch and complain that he could not remember what I had said.

On superficial examination he seemed to understand what was said to him and choose all the common objects accurately to oral command; with colours he was not so exact. But he made gross mistakes, in setting the clock and in carrying out the hand, eye and ear test to orders given by word of mouth. His greatest disability appeared when he was asked to render the general sense of some story I had told him; after the first few phrases, he broke off, saying, "I don't know what it is."

He chose common objects with ease to printed commands and made no gross errors in the selection of colours. The hands of the clock were ultimately set correctly and the hand, eye and ear tests perfectly executed. His difficulty lay not so much in understanding the meaning of a word or phrase read silently to himself as in comprehending their general significance.

He wrote his name and address rapidly and with ease. But the names of common objects or of colours were badly written, although the nomenclature was correct, and he made many mistakes, when writing down the time from a clock shown to him. He was unable to round off and bring to a logical conclusion a letter which began intelligibly.

He would copy with ease and certainty, but, when writing from dictation, he tended to shorten the sentence, to omit some part of its content and to substitute words which differed from those said by me.

He counted perfectly up to the seventies or eighties, and then became slower and less accurate. Simple arithmetical exercises were imperfectly carried out and he seemed unable to correct his mistakes.

He drew the rough outline of a jug placed before him and reproduced it almost exactly from memory; but he absolutely failed to draw an elephant to command.

Orientation was defective and he was unable to construct a ground-plan of the ward in which he occupied a bed, although he gave undoubted evidence of the possession of visual images.

These defects in symbolic formulation and expression were unaccompanied by any other signs of gross destruction in the nervous system. Vision was normal and the field of full extent. Movements of the face and tongue were unaffected. There was no paralysis of motion or sensation and the reflexes, including the abdominals and plantars, were equal on the two halves of the body.

In this case profound semantic defects in a left-handed man were associated with a small cortical and subcortical lesion situated in the lower and posterior portion of the right supramarginal gyrus.

No. 8 (figs. 6 and 7) was another excellent example of the same defects of speech. The lesion was, however, more severe and of considerably greater extent than that in either of the two preceding cases; but it is of interest from the point of view of localization, because the superficial area, occupied by the wound of entry, served to unite that of the last patient (No. 5) with that of No. 18, lying over the superior parietal lobule.

No. 8 was struck by a fragment of shell-casing in the left parietal region; this traversed the brain almost directly from side to side, and was removed through a small trephine opening over the right supramarginal region.

When he first came under my care a month later, there was a small pouting wound on the left side, which lay in the centre of a trephined area, measuring 4 by 2·75 cm. This healed in a fortnight. It extended between two points 26 to 29 cm. along the nasion-inion; above it was 2·5 cm. and below 8 cm. from the middle line of the scalp, seen from behind. The opening on the right side, from which the missile had been removed by operation, had healed completely on admission.

When the extent of the trephined area, over the wound of entry, was plotted on the surface of the brain, it was found to occupy the supramarginal gyrus and part of the superior parietal lobule (figs. 6 and 7). The lowest point just touched the site of the lesion in No. 5, and from this the long axis of the oval extended upwards and a little backwards to just beyond the interparietal fissure.

This patient was a splendid example of semantic aphasia, and his condition at various periods has already been summarized on p. 389.

In this case there were other signs of gross injury to the brain, apart from these semantic defects. Four months after he was wounded, he developed epileptiform atttacks, in which he became unconscious, and was slightly convulsed. Under the influence of worry, confusion and noise, these became somewhat frequent; but with treatment and a quiet life in the country they have been greatly reduced in number.

The most striking physical abnormality consisted of defective vision over the right half of the field. His visual acuity was perfect with either eye, but he tended to miss letters towards the right of any line he was reading, unless his attention was concentrated directly upon them. Over the right half of the field a moving object could be appreciated up to the periphery, but a stationary white square was frequently unrecognized. Moreover, if two discs were exposed simultaneously, one to the left and the other to the right of the visual field, he never failed to appreciate the former, though he was frequently uncertain to the right. This condition has remained unchanged to the present time.

On admission, the optic discs were blurred at the edges, showing traces of previous swelling, which had subsided. The pupils reacted well, even when the light was thrown on the affected half of the visual field. Face and tongue moved normally. The reflexes, including the abdominals and plantars, were equally brisk on the two sides. Careful examination failed to discover any affection of motion or sensation.

There were no abnormal signs of any kind on the left side of the body, corresponding to the opening in the right half of the skull through which the foreign body had been extracted.

This young and highly intelligent officer suffered not only from semantic defects of speech, but also from loss of vision of a high cerebral type over the right half of the field. The wound of entry, which was responsible for these signs and symptoms, lay mainly over the supramarginal gyrus, but extended on to a portion of the superior parietal lobule. It was probably the subcortical passage of the bullet that was responsible for the presence of the partial hemianopia.

In the next patient, No. 18 (figs. 6 and 7), the lesion lay somewhat higher than in any other case of this group, occupying mainly the superior parietal lobule; but there was definite evidence of considerable subcortical destruction. The semantic defects were less profound, although he showed a complete hemianopia, and sensibility was slightly disturbed in the right hand.

He was wounded by shrapnel, rapidly became unconscious, and woke to find himself in a Base Hospital. When admitted under my care exactly a month later, no operation had been performed, and the wound consisted of a long granulating area, which, at the site of its maximum breadth, covered a small stellate fracture of the skull. In the centre of this portion opened a small sinus, leading into the substance of the brain.

This orifice was allowed to close; but suppuration continued in deeper parts. Finally, we explored the track and several fragments of bone, lying about 1·5 cm. from the surface, were removed from the subcortical tissues. The wound then became reduced to a minute sinus, extending for 8 cm. downwards, forwards and inwards; this healed completely, seven weeks after the operation, and exactly eight months from the date of the injury.

The position of this opening in the bone could be determined with greater precision in 1921, when he again came under my care; I shall therefore depend on these measurements for localizing the site of the lesion. The wound was then a firm, deeply depressed scar covering a roughly quadrilateral area, where the bone had been destroyed. This measured 2 cm. in either direction, and the superior border reached to 1·25 from the middle line of the scalp; it extended between two points 22·5 cm. and 24·5 cm. along the nasion-inion line.

If this area was plotted on the surface of the brain, it was found to lie over the superior parietal lobule; but, when interpreting the signs and symptoms presented by this patient, we must not forget the definite evidence of subcortical destruction of tissue (figs. 6 and 7).

No abnormality could be noticed in the course of ordinary conversation beyond a certain hesitancy and diffidence in expression. Intonation, the distribution of the pauses, and the syntax of each phrase were perfect; and yet there was a tendency for his talk to die out before it had reached its full logical conclusion. He named correctly and repeated everything he heard with ease. He understood what was said to him and could carry out simple orders, although the more complex oral commands of the hand, eye and ear tests confused and puzzled him. He read silently or aloud, and understood the meaning, if it was simple and not complex. He wrote his name and address correctly, but, when he attempted to write down the gist of what he had been told or had read to himself, he was liable to make curious errors. He wrote with great rapidity, as if afraid of forgetting what he wanted to express. These defects were particularly evident when, after reading a printed paragraph silently, he was told to narrate or to write down what he had gathered from it. He even found difficulty in writing the alphabet, though he could say it correctly. Simple arithmetical exercises were badly performed; in fact, he started in each instance from left to right. It was not the detailed significance of numbers that was at fault, but rather the general conception of the acts of addition and subtraction. Once this had been corrected in his mind the same problems were easily solved. Orientation was not so grossly affected as in some of the other patients of this group; but the plan he drew of the room, in which we had so often worked, was defective, although he could indicate orally the relative position of its salient points. He had great difficulty in formulating the general intention of some act he was about to perform spontaneously or to order; he could not even lay the table with certainty. But he was able to copy simple actions with ease, provided they did not demand recognition of several alternatives. Oral, pictorial, and printed commands suffered to an almost equal extent. He understood straightforward pictures; but those which demanded coherent composition or the simultaneous comprehension of a printed legend, usually failed to convey to him their full meaning. He could play no games with pleasure and disliked puzzles, which confused him.

The other signs and symptoms, pointing to gross destruction in the central nervous system, remained the same throughout the history of the case. He suffered from no fits or seizure of any kind after the wound had finally healed. In 1921, he showed a complete right hemianopia: he was blind to colour, form and movement over this half of the field, and the pupil did not contract to light, thrown on to the nasal side of the right and the temporal portion of the left retina. Face and tongue moved equally on the two sides. Individual movements of the digits could be carried out perfectly with the eyes open; but, when they were closed, the fingers of the right hand performed these finer movements more clumsily and less perfectly than the left. Moreover the digits on the right side were slightly atonic. These defects were obviously afferent in origin and, on closer examination, the power of recognizing posture and passive movement was found to be somewhat diminished. The compass-test, localization, tactile sensibility and discrimination of shape, weight and texture were unaffected. All the reflexes, including the plantars and abdominals, were normal and equal on the two sides.

This perfect example of semantic defects of symbolic formulation and expression was due to injury of the superior parietal lobule, combined with subcortical destruction. Bone fragments driven into the tissues of the brain had led to suppuration, and it is impossible to determine to what extent this subcortical lesion played a part in the speech affection; but it was evidently responsible for the gross hemianopia and probably also for the changes in sensibility.

§ 3.—*The Relation of the Form assumed by the Aphasia to the Site and Nature of the Lesion.*

In each example dealt with in the previous section I have attempted to map out on the surface of the brain the approximate limits of the injury. Since the impact of the blow came from without, the cortex was affected in every case; but in addition all showed more or less evidence of subcortical destruction. In some instances this was severe and of considerable depth; in others the amount of deep structural change must have been comparatively slight.

But, if my contention is correct that such lesions produce their effect by interrupting a highly complicated form of behaviour, the additional presence of subcortical changes is not of fundamental importance with regard to the nature of the manifestations, although it has a profound effect on their severity and duration. Were aphasia due to destruction or ablation of specific centres for speech, strict limitation of the lesion to the cortex would be a necessary preliminary to any attempt at anatomical localization of function. But such conditions have rarely if ever been fulfilled even in the most satisfactory cases where a careful microscopical examination has been carried out. Destruction was sometimes confined to subcortical tissues; but, if it affected the cortex, the deeper structures were almost always more or less involved.

These changes interfere with the orderly march of a highly integrated series of voluntary and automatic processes, which require perfect action of cortical and subcortical mechanisms. Now, in all my aphasic patients with gunshot wounds of the skull the injury of necessity affected the surface of the brain, to whatever depth it may have penetrated. It is impossible, therefore, from such material to deduce any specific difference between the results produced by a cortical or subcortical lesion. We can, however, conclude that the deeper it extended the more severe and lasting was the disorder of speech.

Bearing these facts in mind, can we draw any conclusions from such cases with regard to the relation between the site of the lesion and the nature of the aphasic manifestations? The number of my patients, in whom the injury was sufficiently limited to be of any localizing value is lamentably small; but in all of them the clinical signs and symptoms were worked out with unusual care and they have been under observation for long periods, extending in some instances over many years. This material, though of great scientific value for determining the forms assumed by disorders of speech, is in no sense ideal for anatomical localization. But, with many reservations, I think it is capable of leading us to certain tentative conclusions.

Thus, in all three cases of uncomplicated verbal aphasia, the lesion lay mainly within or beneath the central convolutions. No. 6 was an ideal example; for his wound consisted of a longitudinal incision, 5 cm. in length, which penetrated to the brain and lay over the lower portion of the precentral gyrus. The only abnormal sign, apart from his affection of speech, was transient weakness of the right half of the face and tongue. Motion, sensibility, and the reflexes were entirely unaffected.

No. 20, in whom an extracerebral tumour pressed upon the lower part of the precentral gyrus, is also of interest in this connection. The operation for its removal was followed not only by severe verbal aphasia, but also by motor hemiplegia unaccompanied by any form of sensory disorder. The abnormal physical signs cleared up rapidly and even the affection of speech diminished to a profound degree, although to the end it maintained its specific verbal character.

No. 17 was of much less importance from an anatomical point of view; for, although the superficial extent of the wound fell over the lower portion of the pre- and post-central gyri, the gravest lesion was an abscess in the substance of the brain beneath them. This was responsible for the gross hemiplegia, both motor and sensory, on the right half of the body. But, in spite of the extent of these destructive changes, the aphasia assumed a purely verbal form and passed away almost completely.

So far we are justified in stating that a lesion situated within the lower portion of the central convolutions, or the structures beneath them, is liable to evoke what I have called verbal defects cf symbolic formulation and expression. These parts are not centres for any constituent element of speech; but injury in this region produces defects in the use of language, which tend to assume this specific form.

When we turn to the three traumatic cases of syntactical aphasia, we are led to an equally definite conclusion. Pick [11] has always contended that a disorder of speech, consisting of true jargon, or as he calls it "agrammatism," is associated with lesions of the temporal lobe. With this conclusion I am in entire agreement; all my three patients, who suffered in this way, had lesions of this portion of the brain.

In No. 15, the bullet entered close to the root of the nose and passed backwards through the left temporal lobe to make its exit just above the left ear. The left eye was destroyed, but the field of vision in that which remained showed the upper quadrantic blindness described by Cushing [5] as characteristic for lesions within the substance of the temporal lobe. There was slight paresis of the right half of the face and tongue with an upward plantar response and loss of abdominal reflexes on the same side; but there was no paralysis of the limbs, motor or sensory, at any time. Subsequently the patient developed characteristic seizures, preceded by an abnormal "smell" and associated with a "dreamy state," each of which was followed by some increase in the degree of syntactical aphasia.

In No. 13, the original wound seems to have consisted of two separate perforations of the skull, which led down to independent suppurating foci. Of these, the uppermost lay in the neighbourhood of the central fissure, whilst the lower one fell over the first temporal gyrus and inferior lip of the Sylvian fissure. The nature of the clinical manifestations seemed to indicate that the latter injury was mainly responsible for the affection of speech. But in addition there was slight paresis of the right half of the face and tongue, which rapidly passed away, associated with some weakness and high-grade changes in the postural sensibility of the right hand. The reflexes and visual fields were entirely unaffected.

The lesion in No. 14 fell exactly over the same area on the surface of the brain as that of the lower wound in the previous case. It occupied the first temporal gyrus and fissure of Sylvius, but evidently extended more deeply into the subcortical tissues; for it was associated on the right half of the body with a gross sensory hemiplegia, absent abdominal reflexes and an upward plantar response. At first speech was extensively affected, but finally the aphasia assumed a purely syntactical form. This patient also suffered from seizures associated with a "dreamy state" and an unpleasant taste or smell, so characteristic of lesions of the temporal lobe.

Thus the temporal lobe was the one constant site of the injury in all these cases of pronounced syntactical aphasia (Nos. 15, 13 and 14) and two of them were accompanied by other characteristic signs and symptoms of a lesion in this situation.

So far, the anatomical conclusions to which I have arrived do not diverge materially from those of other observers. Granting that my views of the nature of the clinical manifestations differ fundamentally from those usually held, it is obvious that what I have called "verbal defects" of symbolic formulation and expression comprise the more specific examples of "motor" aphasia and "anarthria" in Marie's sense of the word. These morbid states are notoriously evoked more readily when the lesion falls mainly on the lower half of the central convolutions and the parts which lie immediately beneath them. My three cases bear out this conclusion.

Moreover, true jargon has long been associated with disease of the temporal lobe and this form of defect of speech is comprised amongst the manifestations of syntactical aphasia. This localization is supported by my three examples of gunshot injury, where the loss of symbolic formulation and expression assumed this form.

But, when we consider the effect of lesions situated behind the post-central fissure, the material at my disposal is unsuitable for strict anatomical localization. The injuries were too diffuse and the limits of the various structural areas on the surface of the brain are less easy to define. Clinically, however, there can be little doubt that unilateral lesions situated between the post-central fissure and the occipital lobule, including the supramarginal and angular gyri, are liable to evoke two diverse forms of disorder in the use of language. One group of defects, which I have called "nominal," is shown by difficulty in recognizing the meaning of such symbols as words or figures and by inability to find appropriate names for objects. The other, or semantic form of aphasia, appears as a more general lack of logical sequence in word or deed, accompanied by defective appreciation of the ultimate significance of statements communicated orally, in print, or by means of pictures.

If we first consider the cases which belonged clinically to this semantic group, No. 10 is the most satisfactory from an anatomical point of view. A hand-grenade, exploding prematurely, had produced a small fracture of the skull over the left parietal region. Fragments of bone pierced the dura and produced an injury of the supramarginal gyrus, which did not extend deeply into the brain. The clinical manifestations formed a perfect example of semantic aphasia, uncomplicated by any other signs or symptoms of injury to the central nervous system.

No. 5 was the only example amongst my collection of war injuries where a right-sided lesion in a left-handed man was associated with disorders of speech. A rifle bullet had entered the brain in the neighbourhood of the contingent parts of the supramarginal and angular gyri; it was removed from a depth of about 4 to 5 cm., and the wound healed in a fortnight. Clinically this patient was a perfect instance of semantic aphasia, unaccompanied by any other signs or symptoms of injury to the central nervous system.

No. 8 was an equally characteristic example, accompanied by partial hemianopia. The missile had traversed the brain almost directly from side to side, but I could find no abnormal signs corresponding to the injury of the right hemisphere. The wound of entry, which was responsible for all the morbid manifestations, both of speech and vision, lay over the supramarginal gyrus and part of the superior parietal lobule.

In No. 18, the fourth example of this clinical group, there was definite evidence of subcortical suppuration. The orifice of the small but deep wound had been allowed to close prematurely and, at a subsequent operation, we removed several fragments of bone lying about 1·5 cm. from the surface of the brain. The external injury lay over the superior parietal lobule. Although the semantic defects were less severe than in the other cases, he showed in addition gross hemianopia and slight sensory changes in the right hand.

Thus in all four instances where the disturbance of speech assumed a semantic form the main lesion lay behind the post-central fissure, in the neighbourhood of the supramarginal gyrus and the superior parietal lobule.

Nominal aphasia forms one of the most distinctive abnormalities of speech. But in two only of my patients was the condition due to injury of the skull and in one of these the area of destruction was too wide to be of any value from the point of view of anatomical localization.

In No. 7, the wound was an arrow-shaped fracture, about 4 cm. by 2 cm., which lay over the angular gyrus. Beyond the nominal aphasia, he showed no signs or symptoms pointing to injury of the central nervous system.

No. 2 was clinically one of the most perfect examples of this group, and I have watched his progress for nearly five years. But the injury was a widespread fracture of the skull, which covered an area corresponding to the angular gyrus, superior parietal lobule and arcus parieto-occipitalis; its anterior border extended as far forwards as the middle of the supramarginal gyrus. We must, however, bear in mind that this gives the extreme limits of the injury within which the destruction of brain tissue occupied an unknown but smaller extent. The lesion extended sufficiently deeply to produce a complete right hemianopia; but there were no further abnormal signs or symptoms.

No definite anatomical conclusions of differential value can be deduced from these examples of semantic and nominal aphasia. Both forms of defective use of language can be evoked most readily by injuries which fall over an area lying between the post-central and interparietal fissures, that is, over the supramarginal and angular gyri and the parts beneath them. But it would seem as if a lesion producing nominal aphasia tended to lie somewhat farther back than one which was associated with semantic disorders of symbolic formulation and expression.

Chapter IV.—General Conclusions and Summary.

§ 1.—*General Conclusions.*

The use of language in its various forms is acquired during the life of the individual, and finally comprises a number of habitual actions, mental and physical, which can be modified at will. An act of speech is a march of events, where one changing condition passes insensibly into another. When speech is defective, this easy motion or transition is impeded; one state cannot flow into another because of some mechanical imperfection in the process. The power of finding words, the rhythmic modulation and balance of a phrase, the appreciation of meaning and intention, verbal or general, are thrown into disorder.

The processes which underlie an act of speech run through the nervous system like a prairie fire from bush to bush; remove all inflammable material at any one point and the fire stops. So, when a break occurs in the functional chain, orderly speech becomes impossible, because the basic physiological processes which subserve it have been disturbed. The site of such a breach of continuity is not a "centre for speech," but solely a place where it can be interrupted or changed.

But the term has been habitually employed in a more inclusive and different sense. Cortical "centres" for motion, sensation or speech are supposed to be areas on the surface of the brain within which certain forms of neural activity are originated. A function is "localized" in a more or less restricted group of cells, and ablation or injury in this region destroys the power to generate the "energy" requisite for some particular form of behaviour. This view is a heritage from the doctrine of "faculties," reinforced by the results obtained on experimental stimultion of the cortex.

Most so-called "centres" in the nervous system are strictly speaking nodal foci, where central neural activities undergo integration and other changes in relation to one another. Like the points on the railway, they determine the subsequent course of events. This may happen automatically or voluntarily, just as the passage of a train may set the track for its successor, or the mechanism may be manipulated at the will of the man in the signal box in response to information received from without. Such a "centre" also forms a shunting station where one group of impulses is guided in one direction, whilst another passes on into some fresh combination.

Whenever a primitive function is rendered more perfect and is given a wider range of purposive adaptation, the structures which are primarily responsible for its existence become linked up with those on a higher anatomical plane of the nervous system. But many of the more mechanical processes and the actual force expended may still be furnished by the lower functional levels. No fresh "energy" is generated by this higher integration, but the response gains in freedom; it can be more closely regulated according to the needs of the moment and brought into harmony with the reaction of the organism as a whole. This is the purpose of that series of complex integrative changes which start with the birth of afferent impressions at the periphery and continue until their ultimate consequences act on the final efferent path.

Speech, reading and writing are acquired at a period when the central nervous system is structurally complete. They require the perfect interaction of widely different forms of behaviour, both psychical and somatic, combined at the moment to a single end. There is nothing exclusive about acts of symbolic formulation and expression; they employ highly integrated functional arrangements, developed originally for other simpler purposes. These in turn depend on the integrity of a series of arcs or circuits, subserving processes on the most diverse physiological levels, the highest of which are to be found in the cortex.

Even motor reactions, aroused by electrical stimulation, consist of a march of events with a definite temporal relation; for the response obtained at any one moment depends on what has happened before. Motor "centres," even in the cortex, cannot be the sole and primary foci from which movements are initiated and determined; they form rather the means by which we are enabled to interfere with otherwise automatic acts, modifying them in accordance with our voluntary requirements. Their function is that of a switch, facilitating, diverting, or even reversing the habitual course of events. Injury or destruction interrupts these processes for a time; but readjustment occurs if the lesion has not been too extensive or profound. Although the "centre" has been completely removed, the movement can be performed, perhaps a little more slowly and uncertainly, but otherwise with no noticeable defect.

The structural mechanism required for the normal use of language not only comprises parts of the cortex exercising functions of various levels in the neural hierarchy, but also requires the synergic activity of centres on a deeper anatomical plane. A lesion at some appropriate place on the surface of the brain can interrupt speech for a time. Sooner or later the flow is re-established; but, the deeper and more acute the injury, the greater will be the severity and duration of the disturbance. The reaction tends to assume a stereotyped form; it is evoked slowly and after an undue expenditure of effort. The deeper the destruction of tissue, the greater is the resistance interposed between the initiation and completion of the processes required for some particular act of speech.

The power to express ourselves in spoken words is acquired by voluntary effort, but ultimately becomes almost automatic. In the same way, when learning to play the piano, the fingers are at first laid laboriously on each key, and a complicated apparatus is thrown into action, which sounds the note. Soon, with practice, the fingers move automatically and consciousness is occupied in reading the musical symbols on the printed page. Finally, with increased facility, even this becomes almost automatic; the expert musician scarcely sees the page, for the nature of the musical phrase suggests to him the sequence of the accompanying harmonies.

Any high-grade aptitude, such as the use of language, acquired by conscious effort, is carried out with practice more and more unwittingly and the functional adaptations on which it relies become gradually engulfed in the automatic activities of the central nervous system. As this habituation proceeds, the particular mode of behaviour in question depends to an increasing extent on the orderly sequence of a series of predetermined reactions. Gross organic injury does not remove the structural basis of a "faculty" or the repository of "images," but disturbs the march of events necessary for the perfect accomplishment of some acquired act; this can be relearnt, even after ablation of the whole of its "cortical centre."

The form and extent of the disorder of function depend on the stage in the life of the individual at which this mode of behaviour was developed; more recent aptitudes suffer in excess of those acquired earlier in ontological history. Each human being learns to speak and to understand what is said to him during his earliest years; the arts of reading and writing, on the other hand, become possible only after he can already express himself fluently in words, and the vast mass of mankind remain permanently illiterate. Anything which disturbs the free use of language will therefore tend to affect the power of reading and writing to a profound degree. Articulated speech, the oldest acquisition racially and individually, exhibits the most specific and particular changes, whilst the recently developed powers of reading and writing are more massively and indifferently affected. The condition of articulated speech and the power of comprehending spoken words are therefore the best indication of the form assumed by an aphasia, and the names I have selected have been chosen to characterize this aspect of the disorder.

These diverse defects of speech do not reveal the elements out of which the use of language is built up; on the contrary, they show the way in which a highly complicated series of acts can be disturbed by lesions of certain parts of the brain. It is the custom to assume that, when some particular form of behaviour is thrown into disorder, the manifestations reveal the functions which combined for its development, exactly as a chemical salt can be analysed into an acid and a base. But in most instances this is not true, as far as the negative phenomena are concerned; they are morbid variants of the disturbed form of behaviour.

Although the negative effects of a lesion are expressed in terms of the affected process, the positive manifestations may reveal activities which under normal conditions are controlled or suppressed. A glass fire-screen allows the light to pass, but shuts off most of the heat. Should it be broken, the fragments do not reveal the elements out of which it was made, though it may be possible empirically to determine that one came from the upper, another from the lower corner. On the other hand, removal of the obstructing pane of glass now permits the heat of the fire to radiate freely into the room. The various forms of aphasia, being for the most part negative effects of the lesion, show how the use of language can be broken up rather than the elements out of which it is composed.

The more definitely the injury destroys the lower portion of the pre- and post-central convolutions and the parts which lie beneath them, the more likely are the defects to assume a "verbal" form. A lesion in the neighbourhood of the upper convolutions of the temporal lobe tends to produce "syntactical" disorders of speech. Destruction round about the region of the angular gyrus causes lack of appreciation of general symbolic significance and intention, defects which I have called "semantic." A lesion situated somewhat more posteriorly seems to disturb the power to discover, to understand, and to employ names and other nominal expressions.

No one part of this wide area on the surface of the brain is associated exclusively with the processes of speech; activities of a lower order can be disturbed coincidently with the use of language. Thus, a lesion of the precentral convolution on the left side not only produces verbal aphasia, but is accompanied in the acuter stages by defective movements of the face and tongue. But these various disorders belong to different levels of functional integration and the term "motor" cannot be transferred from the defective movements to the lack of ability to employ verbal symbols. Moreover, the two disorders of function obey Jackson's law, in that motion returns to the face and tongue before the more highly integrated and recently acquired power to employ words in speech.

§ 2.—*Summary.*

(1) Speech and the use of language in its widest forms require the perfect performance and interaction of a series of processes of great complexity. Acquired during the life of the individual, these are perfected by voluntary effort, and finally come to consist of the orderly exercise of functions, conscious, subconscious and wholly automatic, all working together in harmony.

(2) Once acquired, this form of behaviour can be disturbed by anything which interrupts the orderly precision of the physiological processes on which it depends.

(3) The resulting loss of function is expressed in terms of the complete act, and does not reveal the "elements" out of which it is composed or developed.

(4) To the group of functions which suffer in these high-grade

disorders of speech I have applied the term "symbolic formulation and expression." This is a purely empirical designation, chosen to signify that the power to manipulate such symbols as words and numbers is most profoundly affected.

(5) Acts of symbolic formulation and expression are built up on a level of integration superior to that of motion, and are of a higher order than sight or hearing. Consequently, the clinical manifestations cannot be classified as "motor," "visual" or "auditory" defects of speech.

(6) Moreover, the clinical facts entirely fail to bear out the contention that the various forms assumed by these disorders of the use of language can be classified in distinct categories as faults of speaking, of reading, or of writing. These are purely linguistic terms for diverse forms of human behaviour, and do not even correspond specifically to groups of psychical functions.

(7) There are no "centres" for speaking, reading, writing or other forms of behaviour comprised in the normal use of language.

On the other hand, there are areas of the brain within which structural injury can produce disorders of symbolic formulation and expression. This is manifested in diminished capacity to employ words and figures in certain ways and under certain definite conditions.

(8) The form assumed by an aphasia may differ with the site of the lesion. The structural injury interrupts in various ways the sequence of complex processes necessary for orderly speech, and so produces diverse clinical manifestations.

If it falls over the lower portion of the central convolutions and the parts beneath them, the patient has difficulty in finding verbal forms in which to express his thoughts. Injury to the temporal lobe, on the other hand, leads to disordered rhythm and want of grammatical structure ; speech tends to become true jargon. A lesion lying between the post-central fissure and the occipital lobule disturbs the appreciation of meaning, either verbal or general. In the first case, it is mainly the nominal value of words which suffers ; in the latter, the patient finds difficulty in recognizing the ultimate significance of logical conceptions evolved by himself, or placed before him orally, in print or in pictures.

(9) Cortical and subcortical mechanisms participate in every act of language. The deeper a lesion extends from the surface into the substance of the brain, the more definite and permanent will be the disorders of speech.

(10) Acuteness of onset has a profound effect on the severity and nature of the morbid manifestations. A small destructive lesion,

arising suddenly, may produce a greater loss of function than one of wider extent but slower incidence. Should the structural changes remain quiescent, readjustment of function can occur, and signs and symptoms tend to diminish or pass away. They may reappear under the influence of fatigue or any event which lowers neural capacity, such as an epileptiform seizure.

APPENDIX.

I have selected for fuller description five characteristic cases from amongst those mentioned in the text. In the present paper I have dealt solely with patients where the affection of speech was due to an injury, because I was able in every such instance to obtain some approximate evidence of the site of the lesion. But my views on the clinical forms and nature of aphasia are also based on a series of non-traumatic examples, which I hope to describe later.

§ 1.—*A Case of Acute and Severe Verbal Aphasia, due to the Removal of an Extra-cerebral Tumour, followed through Various Stages of Recovery.*

No. 20.—Alice Lucy Esther B., a widow lady of 56, first came under my care on May 29, 1922, complaining of epileptiform convulsions.

In 1916 she went to bed one night at 10 o'clock apparently in perfect health. As she was falling to sleep, she suddenly felt that she could not use her right hand, particularly the thumb and index finger. She sprang up in bed with a sensation of choking and became unconscious, passing urine involuntarily. Two months later she had an exactly similar attack, and in the course of the last six years lost consciousness six times in all. But from time to time she has suffered from minor seizures, which began with a "numb feeling" in the thumb ; the tip then became flexed towards the palm, the digits "drew up" and she was unable to open them. Then the face might become affected ; but if the hand was rubbed vigorously the attack would often come to an end without loss of consciousness.

The last seizure, which was a slight one, occurred on May 20, 1922, and began with the usual symptoms in the thumb and index finger of the right hand. She did not become unconscious, but for six or seven hours afterwards her speech was affected and she was unable freely to express her wishes ; by 3 a.m. she had entirely recovered. This loss of speech so greatly alarmed her that she determined to consult a specialist.

When she first came under my care she was an extremely vigorous woman, who not only managed a large household, but carried on with success the business of a decorator and paper manufacturer.

Her pulse was normal, except that the tension was distinctly high (diastolic 120 mm., systolic 190 mm.). The heart was unaffected. Her urine was of a specific gravity of 1020 and contained no albumin or sugar; but in the past she had suffered from glycosuria, which, however, could be completely controlled by a moderate restriction of diet.

A shrewd, capable, North-country woman, her intelligence was much above the average and her mental state had remained unchanged by her illness. Speech had not been affected except during the last attack. She told me: "I knew what I wanted to say, but I could not explain it to anyone; I couldn't seem to put the words together and I couldn't have made a long sentence." When she came under my care, speech, reading and writing were in every way perfect. She carried on her business, kept accounts and made all the arrangements for her stay in London unaided with ease and assurance.

She denied that she ever suffered from headache, but complained of an unpleasant sensation, which was "not a pain," behind the eyes and over the vertex. This was increased by stooping or by worry, though not by intellectual efforts or physical fatigue. At no time had her head been sore or tender. She had vomited after the attacks in which she became unconscious, but had not otherwise suffered even from nausea.

Vision was $\frac{6}{6}$ in either eye and the fundi showed no changes of any kind. Hearing, smell and taste were excellent in every way.

The pupils reacted well, ocular movements were perfectly executed and there was no nystagmus. The face moved equally on the two sides: the tongue was protruded straight and withdrawn without deviation.

The right wrist-jerk was somewhat brisker than the left, but the knee- and ankle-jerks were normal and both plantars gave a downward response. In consequence of the laxness of the abdominal wall, the reflexes were obtained with difficulty even to the left of the middle line; on the right side I could not elicit them at any time.

There was no paralysis, paresis, tremor or inco-ordination. Individual movements were as well executed by the digits of the right as by those of the left hand, and their tone was in no way affected. Her gait was normal and she could stand equally well on either foot with the eyes open or closed.

The most careful sensory examination failed to reveal any disturbance of sensation. Her power of appreciating the tactile hairs, weight, form, texture, measured movements and the two compass-points was equally good on the two sides, and localization was perfect.

From these signs and symptoms I concluded that she was suffering from the effects of a tumour, probably of extra-cerebral origin, within the left half of the cranial cavity. The absence of sensory defects in the period between the attacks led me to believe that it was situated in front of the fissure of Rolando.

On June 20, 1922, Mr. Wilfred Trotter removed a smooth, lobulated, fibrous growth, which measured 5 cm. antero-posteriorly, 4 cm. vertically and 3·5 cm. in depth. Microscopically its structure was that of a fibro-endothelioma. It sprang from the dura mater, which was in turn firmly attached to the bone above it; this was soft and vascular, cutting like cheese. The tumour was so carefully extracted that not even the smallest fragment of cortical tissue adhered to the mass removed. The depression it had produced in the substance of the brain seemed to be centred around the meeting point of the inferior frontal and the inferior precentral fissures.

The wound healed by first intention and the patient showed no evidence of surgical shock or other unpleasant manifestations. But on the day after the operation she was speechless except for the words "yes" and "no"; and even "no" was sometimes wrongly employed, when she intended to express assent. This aphasia was accompanied by complete flaccid hemiplegia on the right side of the body with paralysis of the same half of the tongue and lower part of the face. The right plantar reflex gave a definite upward response, and arm- and knee-jerks were brisker than those on the normal side.

From this time onwards she improved steadily day by day both physically and in her powers of speech. As the interest of this case lies more particularly in the order and manner of her recovery, as revealed by systematic examination, I shall divide my report into two portions, the first of which narrates the restoration of her physical powers, whilst the second deals with the much slower return of symbolic formulation and expression.

Physical Examination.

On the *fourth day* after the operation (June 24) she had recovered considerable strength in the right leg, and could even dorsiflex and plantar extend the right foot. Some power had returned at the shoulder and elbow, and, although individual movements of the digits were impossible, she could close the fingers over mine in a feeble grasp. The lower portion of the right half of the face was completely paralysed, and the tongue deviated grossly to the same side on protrusion. All the deep reflexes on the affected half of the body were brisker than those on the left side; and the right plantar gave a characteristic upward response.

On the *sixth day* (June 26) power had returned to a remarkable extent; she could make individual movements of the fingers and thumb of the right hand, and the grasp, though weaker than that on the normal side, had greatly increased in strength. All movements were now readily performed by the right leg. Some slight motion had returned to the right half of the face, and the tongue was protruded more nearly in the middle line; she could now lick the right angle of her mouth with ease. The right wrist-jerk was brisker than the left, but the knee- and ankle-jerks were equal on the two sides. On scratching the sole of the right foot, the great toe remained stationary, whilst the others moved downwards and became approximated to one another; similar excitation of the normal foot led to brisk downward movement of all the toes. I could not obtain the reflexes from the right half of the abdomen; but even those on the normal side were doubtful, probably owing to the laxity of the abdominal wall.

On the *seventh day* (June 27) every movement of the right lower extremity was perfect, and crude power had almost completely returned to the right hand. When the arm was held out in front of her, the fingers were in alinement with one another, and they did not fall away on closing the eyes. The lower part of the right half of the face acted voluntarily, though less perfectly, than the left, and the tongue was protruded in the middle line. I could discover no sensory loss of any kind. She could appreciate passive movements of 2° in all the digits, and answered "front" or "back" correctly. She had no difficulty in recognizing the shape of solid geometrical objects placed in the right hand, and nothing pointed to any "stereognostic" defect.

On the *tenth day* (June 30) power had greatly increased in the whole of the right upper extremity; individual movements of the fingers and thumb were now possible, and the grasp of the right hand equalled that of the left. The lower portion of the right half of the face was still weaker than the opposite side, but the tongue was protruded in the middle line, and did not deviate on retraction into the mouth. The right wrist-jerk was brisker than the left, whilst the knee- and ankle-jerks were equal on the two sides, and the right plantar gave a completely normal response. Her power of appreciating geometrical shapes was again tested and found to be perfect with either hand.

On the *fourteenth day* (July 4) the grasp of the right hand was stronger than that of the left, and individual movements of the digits were equally well performed on the two sides. There was no inco-ordination or ataxy, and the fingers did not fall out of alinement when the eyes were closed. The two wrist-jerks were now equal, and the right plantar exactly resembled that obtained from the normal foot. I was able to elicit a slight reflex from the upper half of the abdomen to the right of the middle line, though not from parts below the umbilicus; but it must be remembered that these reflexes were obtained with great difficulty even on the normal side.

On the *sixteenth day* (July 6) I could find no definite physical signs pointing to loss of function in any part of the nervous system. The patient was free from headache or discomfort; even the opening in her head did not trouble her. Vision was unaffected, the fields were not restricted, and the fundi normal. The pupils reacted well and movements of the eyes were perfect in all directions. The right half of the face moved well, and I could not observe any difference between the two sides. The tongue was both protruded and withdrawn in the middle line. Motor power of both upper and lower limbs, including individual movements of the fingers, was completely restored, and there was no sensory loss of any kind. All the reflexes, except those from the abdomen, were normal and equal on the two sides.

Thus, at the expiration of sixteen days after the removal of an extra-cerebral tumour in the left frontal region, a complete flaccid hemiplegia affecting the face and tongue had cleared up entirely, and no definite difference could be discovered between the reaction of the two halves of the body.

Symbolic Formulation and Expression.

At first she was speechless except for "yes" and "no"; and even "no" was at times wrongly employed. Told to give me her hand or touch her nose, she could do so, but became confused if I specified either the right or the left hand. She seemed to understand simple orders, such as to turn over in bed or move the arm or the leg, but she frequently failed to comprehend the full significance of questions, and was profoundly puzzled by her inability to express her wants.

By the *sixth day* (June 26) her speech had greatly improved, and she used "yes" and "no" appropriately. She asked spontaneously for an "orange" and for "tea," and employed the following phrases: "I know well enough," "Can't say well enough," "I don't know—no." Asked what she thought of the flowers in her room, she said: "Very pretty, very pretty." She spoke extremely slowly, and evidently formed the words with difficulty; those of more than one syllable tended to be slurred, or were divided by a pause of considerable length into two parts.

She understood simple statements, but was liable to become confused if the words implied a complex order. Told to touch her nose with her right or her left hand, she did so correctly four times in succession; but, when asked to touch her nose or her eye with one or other hand, which introduced a double choice, she failed in four out of eight attempts.

A request to name coins placed before her led to the following result:—

A penny	"quinny"
A shilling	"sixpence"
A halfpenny	correct
A two-shilling piece ...	correct
A sixpence	correct
A penny	correct
A shilling	correct
A halfpenny	"sixpence, halfpenny"
A two-shilling piece ...	"Jew shill-ns"
A sixpence	correct

Asked to name the relative value of two coins laid on the table together, she gave the following answers:—

A sixpence and a shilling	"sixpence"
A penny and a shilling	"sixpence, shill-en, two shillings, you know . . . eleven"
A penny and a sixpence	"fivepence"
A shilling and a two-shilling piece ...	"one and six"
A sixpence and a two-shilling piece ...	"sixpence, shill-en"
A halfpenny and a penny	"shill-en"

On the *seventh day* (June 27) I was able to test her with a set of familiar objects in the usual way. (See Table I.)

Asked to point to the object on the table which corresponded to the one shown to her or placed in her left hand out of sight, she had not a moment's doubt, but made her choice with great rapidity; the act of matching was evidently performed with ease. She also chose correctly, though more slowly, to an oral command and, when it was given in the form of a printed word, she made two mistakes only. Out of eighteen attempts to name these objects, she was completely successful in ten, and most of her failures were due to defective word formation; the sounds she uttered bore a definite relation to the word she was seeking. Thus she said "match-er," "match-ox," and "match-oz," for match-box, and "pea-ny" or "pence" for penny. Told to repeat the names after me, her enunciation was better, although she still showed some difficulty in verbal formation. When she attempted to write them down without saying them aloud, most of the words bore some relation to the usual designation of the object before her; but they were extremely poorly written and spelt. The individual letters were badly formed and the structure of the words was defective. This was the case, even when she copied them from print in cursive handwriting.

TABLE I.

	Pointing to object shown	Naming object indicated	Oral commands	Printed commands	Duplicate placed in hand out of sight	Repetition	Writing name of object indicated	Copying from print
Knife	Perfect	Correct	Correct	Correct	Perfect	Correct	rib	Knive
Key	,,	,,	,,	,,	,,	,,	Beeg	Gey
Penny	,,	,,	,,	,,	,,	Punny	penney	Tenny
Matches	,,	Matcher	,,	,,	,,	Correct	Mahickes	Mahickes
Scissors	,,	Correct	,,	,,	,,	,,	Secissors	Ssuccoors
Pencil	,,	,,	,,	,,	,,	,,	peicel	Penceil
Key	,,	,,	,,	,,	,,	,,	Bey	Key
Scissors	,,	Key; corrected	,,	,,	,,	,,	Sicissors	Scissors
Matches	,,	Match-ox	,,	,,	,,	,,	Martchs	Matchers
Knife	,,	Correct	,,	,,	,,	Knive	Bnife	Knife
Penny	,,	Pea-ny	,,	Pencil	,,	Correct	peinny	Penny
Matches	,,	Match-oz	,,	Correct	,,	,,	Matches	Mahches
Scissors	,,	Correct	,,	,,	,,	,,	Scissars	Ssissors
Pencil	,,	No answer	,,	,,	,,	,,	pencel	Penceil
Penny	,,	Pence	,,	Pencil	,,	,,	penny	Penney
Knife	,,	Correct	,,	Correct	,,	,,	Knife	Knife
Key	,,	,,	,,	Knife; corrected	,,	,,	guey	Key
Pencil	,,	Knife; no, pencil	,,	Correct	,,	,,	pencel	Pencel

Moreover, a characteristic incident occurred at the beginning of the written portion of these tests. After explaining to her that she was to write down the name of each object as it was shown to her, I handed her a block of paper, which I had headed with the word "writing"; this exercised a fatal attraction, and she insisted on copying it instead of recording the name of the object she had just seen. I tore off the sheet, and she began the new one with the same word, but finally after another explanation she started to carry out the task I had set her. This is a good example of the verbal perseveration, which is so liable to disturb the records in this class of disorders of speech.

On the same day I tested her with the alphabet. She said the letters spontaneously in due order up to "N," added "V" "P" and then stopped. She made a fresh start and again ran correctly up to "N": after a pause she continued "P Q R S T U V," and with the exclamation "I can't say it," gave up altogether. But, when I said the alphabet, she could repeat it accurately letter by letter. Asked to write the alphabet spontaneously, she produced the following series: A B C D E T G H I S B J L M M C P q B S t u v w X Y Y. She had great difficulty in copying capitals in cursive script; in fact every letter up to "I" was copied exactly, and she then continued:—

(The copy) J K L M N O P Q R S T U V W X Y Z.
(She wrote) 5 4 4 m m o p y T s t U U W X Y ʒ.

On the *tenth day* (June 30) I carried out a complete series of hand, eye and ear tests with the following result:—

TABLE II.

	Imitation of movements made by the observer	Imitation of movements reflected in mirror	Oral commands	Printed commands	Writing down movements made by the observer
L. hand to L. eye ..	Correct	Correct	Correct; slow	Correct; slow	right eye
R. hand to R. ear ..	Reversed	,,	Correct	R. hand to L. ear	right eye
R. hand to L. eye ..	,,	,,	,,	R. hand to L. *ear*	right eye
L. hand to R. eye ..	,,	,,	R. hand to R. eye	L. hand to R. *ear*	left eye
L. hand to L. ear ..	,,	,,	Reversed	Correct	left Eay
R. hand to R. eye ..	L. hand; corrected	,,	Correct	,,	right Eye
L. hand to R. ear ..	Correct	,,	Reversed	,,	left Esey
R. hand to L. ear ..	,,	,,	Correct: slow	,,	right ear
L. hand to L. eye ..	Reversed	,,	Correct	L. hand to R. *ear*	left Eye
R. hand to R. ear ..	,,	,,	R. hand to L. ear	Correct	left Ear
R. hand to L. eye ..	Correct	,,	Correct	,,	right eye
L. hand to R. eye ..	L. hand to L. eye; corrected	,,	R. hand to R. eye	,,	"Can't"
L. hand to L. ear ..	Reversed	,,	L. hand to L. *eye*	L. hand to R. ear	Illegible
R. hand to R. eye ..	R. hand to L. eye	,,	Correct	Correct	,,
L. hand to R. ear ..	Correct	,,	,,	,,	,,
R. hand to L. ear ..	,,	,,	,,	Reversed	,,

There was no question that she understood what she was asked to do, although she was occasionally slow in beginning some new form of these tests. Sitting face to face, she succeeded in imitating my movements correctly in eight out of sixteen attempts; in seven her response was an exact reversal, and she made one complete mistake only. But, when they were reflected in the glass, she did not hesitate for a moment. Both oral and printed commands were badly executed, and with the latter she substituted ear for eye on three occasions. Asked to write down my movements, sitting face to face, she simplified the task by naming the right or left hand, omitting any indication of which eye or ear I had touched. This was evidently a severe test, and towards the end her writing became illegible.

She had great difficulty in writing her name and address both spontaneously and to dictation. Not only were the letters badly formed, but some were omitted, whilst others were duplicated, and the whole was illegible except on careful analysis.

On the *fourteenth day* (July 4) her speech had greatly improved. She gave her name and full address correctly, and with almost perfect enunciation. She talked very slowly and with evident difficulty in finding words; but the nurses insisted that she knew exactly what she wanted. She said to me: "I . . . been . . . inkin . . . improvement" (I've been thinking there has been improvement).

I asked her to repeat three short sentences after me one by one; this she did correctly as follows:—

"I have been getting better day after day"; "And I have no sickness or headache"; "I was allowed to sit up to have my bed made yes-day af-er-noon" (yesterday afternoon). Told to repeat them as a single sequence, she was unable to do so, saying "I was allowed to have my bed made yes-day after-noon . . . No, I can't." I then said all three phrases together, but she failed to repeat them, saying "I was allowed to . . . to have my head . . . Why I ought to say that . . . I was allowed."

She wrote her name and address spontaneously as follows:—

Alicce Lucy Esther B.
16 West Vi er
Bark Pa
Barnsleey.
(Alice Lucy Esther B.
16 West View,
Park Road,
Barnsley).

I printed her name and address and asked her to copy it; but instead of reproducing it letter by letter, she glanced backwards and forwards from the print to the paper and wrote down what she had gathered. The result exhibited exactly the same kind of mistakes as her spontaneous writing; words and letters were so badly formed as to be in places almost illegible. Asked to write anything she wished to tell me, she produced with difficulty and many erasures and corrections, "think have been gettig againg allrthat" (I think I have been getting allright) and "I have been going to have." Asked to interpret these scrawls, she said "I have been going to say that I have been . . . I told a sister that . . . ."

I then examined her with the clock tests and obtained the following results:—

TABLE III.

	Direct imitation	Telling the time	Clock set to oral commands	Clock set to printed commands	
				Ordinary nomenclature	Railway time
5 minutes to 2 ..	Correct	Correct	Correct	Correct	Set 12.40
Half past 1 ..	,,	,,	,,	,,	Correct
5 minutes past 8..	,,	,,	,,	,,	,,
20 minutes to 4 ..	,,	"Quarter to 4; 5 and 20 to; 10 minutes to 4"	,,	,,	Set 2.40
10 minutes past 7	,,	Correct	,,	Set 10.10	Correct
20 minutes to 6 ..	,,	,,	,,	Correct	Whispered "5.40." Set 4.50
10 minutes to 1 ..	,,	,,	Set 10 minutes past, but hour hand before 1	Set 10 to 10	Correct
A quarter to 9 ..	,,	,,	Correct; slow	Correct	,,
20 minutes past 11	,,	"5, 10, 15, 20 past 11"	Correct	,,	Set 10.40
25 minutes to 3 ..	,,	Correct	Set 20 minutes to 3	,,	Correct

She was remarkably bright and cheerful, but was puzzled by her failure to express herself and was liable to become confused. When she was right she responded quickly; but, if she made a mistake, she said it over under her breath and usually got wrong again. That is to say she made a mistake, appreciated that it was incorrect and then repeated the order in a whisper or aloud, saying it wrong; on this she acted and fell a second time into error. All her actions seemed to be guided by whispered audible or inaudible words, except when she placed the hands of a clock in direct imitation of one set by me; this she carried out rapidly and her lips did not move. She could tell the time slowly, but on the whole correctly, helping herself by counting on her fingers. With oral commands she was certainly dependent on correct repetition of the words said by me, as far as I could interpret her whispers. Given a printed order in the usual nomenclature, her lips moved and she then set the clock without looking back at the card; the verbal formulation had fixed the task in her mind and she usually succeeded in placing the hands correctly. But she had great difficulty, when the command was printed in railway time; for she tended to set the short hand exactly opposite the hour and then flung the other one into a position corresponding to the number of minutes. Evidently the words "past" or "to," directly preceding the hour, helped her to recognize that the short hand should not be placed exactly opposite the number mentioned in the printed order.

On the *sixteenth day* (July 6th) I again tested her with the alphabet, which she could now say spontaneously without a mistake. Moreover she read it aloud perfectly from print. But, when I gave her the twenty-six block letters and asked her to put them together in order, she said after much

TABLE IV.

	Reading aloud	Reading from pictures	Writing from dictation	Writing from pictures	Copying from print
The dog and the cat ..	Man and the cat	Dog and a cat	The dog & & Cart	Dog Cat	The Dog & the Cat
The man and the dog..	Man and a dog	Man and a dog	The man and the dog	The man & the dog	The man & the Dog
The cat and the man..	The cat and man	Cat and the man	The cat & the man	The cat & the Man	The Cat & the Man
The cat and the dog ..	The cat and dog	Cat and dog	The Cat & the dog	The cal & tthe dog	The Cat & the Dog
The dog and the man..	Dog and the man	Dog and the man	The dog & the man	The & the man	The dog & the Man
The man and the cat ..	A man and a cat	Man and a cat	The man & the cat	The man & the cat	The Man & the Cat
The dog and the man..	A dog and the man	Man and . . .	The dog & the man	The dog & & Manj	The Dog & the Man
The cat and the man..	The cat and a man	Cat and the man	The cat & the man	The cat & the Man	The Cat & the Man

hesitation "I can't find the right letter." She picked out an "I" and slowly selected A B C F, from this she formed the sequence A B C D E F G L and then gave up, complaining "I can't do it." Asked to write the alphabet she produced the following series :—

A B C D E T G H I J B l m m o p q r s t u

After a pause began again spontaneously :—

A B C D E T G H I J B L m m o p q r s t u v w x y ξ.

Each letter was said in a whisper and definitely verbalized. To dictation she wrote the following sequence :—

A B C D E E G H I K L m n o P Q R S F w v w Y z x,

and she copied the alphabet from print in a very imperfect manner.

On the same day I carried out a series of the man, cat and dog tests. (See Table IV.)

She read these simple phrases slowly but correctly and made no essential mistakes, when translating pictures into words ; once only did she fail to complete the couple shown to her. The content of each sentence, written to dictation, was accurately reproduced, but the structure of the words was defective and the letters were badly formed. These faults were even worse when she wrote from pictures. She found much less difficulty in copying from print, although her writing was poor and the letters imperfect, every word was, however, reproduced in cursive script.

On the *twentieth day* (July 10) speech was slow and broken by long pauses, but she volunteered many more remarks. Thus she said, "My head is not . . . quite right . . . it's . . . er, numb . . . otherwise . . . otherwise . . . it will do." Asked to explain her difficulty in speaking, she answered, "My difficulty is . . . I know what I want to say . . . I don't know how to say it . . . Sometimes I feel . . . sometimes I feel . . . if . . . if I . . . if I can't say it . . . I can't think sometimes . . . if I could get my thoughts right . . . I should be allright."

By this time her speech had so greatly improved that the colour tests were carried out correctly, with the exception that she tended to call red "pink" and orange "red." All were selected without fail to oral and printed commands, and she wrote down their names accurately, excepting that she was puzzled by "helitrope" (heliotrope), her designation for violet.

On the *twenty-sixth day* (July 16) she wrote her first spontaneous letter ; it was coherent and reasonable, but many of the words were badly formed. For instance, she wrote, "I am glod Arthrur won the prize for the windom competion" (I am glad Arthur won the prize for the window competition).

I put her through another series of hand, eye and ear tests, and it is interesting to notice the nature of the improvement in these records. (See Table V.)

When imitating my movements sitting face to face, she made fourteen mistakes, but twelve of these were complete reversals in which she selected right for left and vice versa. When she attempted to write them down all sixteen were erroneously recorded ; of these two were reversed, whilst in three she mistook eye and ear. But oral commands were perfectly executed and, when given in print, she made four mistakes only. I then asked her to read them aloud, which she did perfectly, and the errors in their performance were reduced to two. At first she had difficulty in grasping that the printed order read aloud implied an action and was satisfied when the words were uttered; but, if they were read silently, she at once began to carry out some movement of one or other hand.

TABLE V.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Oral commands	Printed commands	Writing down movements made by the observer
L. hand to L. eye ..	Reversed	Correct	Correct	Correct	right to yoo right ear
R. hand to R. ear ..	,,	,,	,,	,,	left to left ear
R. hand to L. eye ..	Correct	,,	,,	,,	left to right eye
L. hand to R. eye ..	Reversed	,,	,,	,,	right to left *ear*
L. hand to L. ear ..	L. hand to R. ear	,,	,,	,,	right to right ear
R. hand to R. eye ..	R. hand to L. eye	,,	,,	,,	left to right Cay
L. hand to R. ear ..	Reversed	,,	,,	L. hand to R. *eye*	right to right ear
R. hand to L. ear ..	Correct	,,	,,	Correct	left to left ear
L. hand to L. eye ..	Reversed	,,	,,	,,	right to right *ear*
R. hand to R. ear ..	,,	,,	,,	L. hand to R. ear	left to left ear
R. hand to L. eye ..	,,	,,	,,	Correct	left to right eye
L. hand to R. eye ..	,,	,,	,,	,,	right to left eye
L. hand to L. ear ..	,,	,,	,,	L. hand to R. ear	right to right *eye*
R. hand to R. eye ..	L. hand to R. eye	,,	,,	Correct	left to left eye
L. hand to R. ear ..	Reversed	,,	,,	L. hand to R. *eye*	right to left ear
R. hand to L. ear ..	,,	,,	,,	Correct	left to right ear

On the *twenty-seventh day* (July 17) she carried out without fail a series of tests with familiar objects, naming them accurately, choosing them to oral or to printed commands and even writing the words correctly. She had now begun to note on paper memoranda of her wants, such as "more diet," "might I have more," "preasure" (pressure) and "tingle," both of which referred to sensations in the head.

On the *thirtieth day* (July 20) I asked her to write her name and address. She did so correctly, no longer in the form of a signature, but as if it stood on the envelope of a letter sent to her home:—

Mrs. J. B.
16 West View
Park Rd.
Barnsley.

I then covered this up and requested her to write her name and add the address of the nursing home; but she repeated her previous performance exactly. When I explained to her that I wanted her address in London, where she had daily received letters from her relatives, she replied, "I can't," and made no attempt to write it. I then dictated it to her word by word and she wrote:—

Mrs. J. B.
The empire nursing hone
Vinsent sq.
Westminster
London S.W.

(i.e., The Empire Nursing Home, Vincent Square, Westminster, London, S.W.)

From the print she copied it as follows:—

Mrs. B.
Ehe empire Nursing Home
Vincent square
Westminsteer E.1111

She was then put through a series of tests with the alphabet. She could now say the letters with ease, both spontaneously and to repetition, and read them perfectly aloud. She wrote them in cursive capitals and her only errors were "T" for F, "B" for R, "J" for T, and the "Z" was given several extra turns. They were written more easily to dictation and she copied them perfectly, in both cases employing small cursive script. I then gave her the twenty-six block letters which, after some hesitation, she finally succeeded in placing in their right order to form a perfect alphabet.

On the *thirty-second* and *thirty-third days* (July 22-23) she was so bright and active that I was able to subject her to a more extensive series of tests.

Her spontaneous speech had still further improved and she attempted sentences of much greater length. For instance: "I went for a drive this morning . . . I enjoyed it more than in fine weather . . . It was a bit dull . . . suited me better . . . For an hour and a half." She was much troubled that her head had been shaved and had ordered a wig; she inquired, therefore, "Might I . . . I shall think of it soon . . . might I . . . wear hair now?" Intonation was still defective, the pauses were multiplied and tended to fall in the middle of a phrase or at the end of a single word. Speech became syncopated with a repetition of rising and falling accents: e.g., "Ĭ $\overline{\text{seem}}$ . . . tō $\overline{\text{have}}$ . . . ă $\overline{\text{weight}}$ . . . ōn $\overline{\text{here}}$" pointing to her head.

She could now name the geometrical shapes placed in her left hand out of sight, calling them respectively "square" (cube), "cork" (cylinder), "marble" (sphere), "nutmeg" (ovoid), "spindle" (cone). With a pyramid she said "oblong . . . can't describe it"; then suddenly she exclaimed "pyramid."

She carried out a complete series of clock tests without a mistake, telling the time correctly and setting the hands to oral or to printed commands, whether they were given in ordinary nomenclature or in railway time. She could even write down the time accurately if she was allowed to intermingle at will figures and words.

The hand, eye and ear tests yielded a much improved set of records. It is true that, when she attempted to copy my movements sitting face to face, she was wrong sixteen times in succession; but of these thirteen were direct reversals and in three attempts only did she mistake the nature of the movement. Oral and printed commands were perfectly executed and she could even write down my actions with four errors only.

TABLE VI.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Oral commands	Printed commands	Writing down movements made by the observer
L. hand to L. eye ..	Reversed	Correct	Correct	Correct	Correct
R. hand to R. ear ..	,,	,,	,,	,,	Left hand to left *eye*
R. hand to L. eye ..	,,	,,	,,	,,	Correct
L. hand to R. eye ..	,,	,,	,,	,,	,,
L. hand to L. ear ..	R. hand to L. ear	,,	,,	,,	,,
R. hand to R. eye ..	Reversed	,,	,,	,,	,,
L. hand to R. ear ..	,,	,,	,,	,,	Reversed
R. hand to L. ear ..	,,	,,	,,	,,	Correct
L. hand to L. eye ..	R. hand to L. eye	,,	,,	,,	Left hand to left *ear*
R. hand to R. ear ..	Reversed	,,	,,	,,	Correct
R. hand to L. eye ..	,,	,,	,,	,,	,,
L. hand to R. eye ..	,,	,,	,,	,,	Reversed
L. hand to L. ear ..	,,	,,	,,	,,	Right hand to left ear
R. hand to R. eye ..	,,	,,	,,	,,	Correct
L. hand to R. ear ..	,,	,,	,,	,,	,,
R. hand to L. ear ..	R. hand to R. *eye*	,,	,,	,,	,,

Observations made from October 20 to 23, 1922, *four months after the Operation.*

She was in excellent physical condition and her urine contained no sugar or other abnormal constituent. The trephine opening was somewhat depressed and pulsated slightly in the sitting posture ; this was considerably increased, when her head was lowered, but was scarcely perceptible after lying horizontally for a considerable period. She complained of no headache or tenderness, superficial or deep, and had suffered from no fits or seizures of any kind.

Except for her disturbance of speech, I could discover no abnormal signs pointing to any affection of the central nervous system. Movements of the face were carried out equally well on the two sides and the tongue was protruded in the middle line. All the reflexes were normal, including the plantars ; I could even obtain a response from the right half of the abdomen and there was no longer that difference on the two sides, which constituted the earliest and most lasting sign of disease. The grasp of the right hand was stronger than that of the left and individual movements of the fingers were perfectly performed, both the eyes open and shut. The right lower extremity had recovered completely and she could walk three miles without undue fatigue. The most careful sensory examination failed to reveal any abnormality ; size, shape, and weight were appreciated equally well with either hand.

Symbolic Formulation and Expression.

She was bright, gay, pleased to come to London and anxious to enjoy its sights. So great was her energy, that it was difficult to prevent her from tiring herself unduly and all my observations were made in the morning in the quiet surroundings of my consulting room.

Articulated speech.—In spite of profound recovery her speech showed the same defects as before, though to a much slighter degree. She now talked easily, her enunciation was greatly improved and the pauses occurred at longer intervals; yet, in principle, the defects were of the same kind as before. She was conscious that her speech lacked freedom; she had no difficulty in finding names, but the words were pronounced slowly and the form of the phrase, though it remained essentially grammatical, was frequently altered to obviate verbal difficulties. Thus she said "Doctor Head . . . should my head have a big dint in it . . . if I lie down . . . for an hour or two . . . the dint is not there . . . but if I sit up . . . any time . . . a big dint is there . . . I asked my doctor . . . he said . . . it didn't matter . . . I didn't know . . . you . . . had . . . cut so much out . . . until I got home." All her faults depended on inability to discover the exact verbal form she required. If, however, she stumbled over a word, she was loath to leave it uncorrected and had a strong sense of her errors in articulation.

She showed exactly the same defects of speech, when she attempted to repeat a series of phrases said by me, hesitating over such words as "elephants" and "zoological." She did not slavishly follow each individual word, but evidently formulated the meaning to herself and then attempted to express it. This led to the same difficulties as when she talked spontaneously, though every point of importance was correctly seized and she omitted no essential detail.

Understanding of spoken words.—She understood everything that was said to her and carried out oral commands perfectly. She could follow and take her part in general conversation, provided she was not hurried.

Reading.—Printed commands were correctly executed and she gave a good account of the contents of a paragraph she had read silently. Moreover, she could interest herself in a book, although she no longer read aloud as had been her custom before the operation. Asked to read aloud a selected passage, she succeeded in pronouncing all the words, although she stumbled over many of them and corrected herself in exactly the same way as with spontaneous speech.

Writing.—She could write a coherent letter and express herself spontaneously in writing. The only noticeable defects were hesitation and uncertainty over the form of some of the letters or component parts of a word; but she was always able, on reading over what she had written, to detect these errors and to make the necessary corrections. Asked to write down what she had gathered from a selected passage, the contents were given correctly, but the form of the words was defective and the spelling was extremely bad. Throughout, her lips moved silently and she was evidently saying the words to herself, although I could detect no sound.

Exactly the same faults appeared, when she wrote to dictation, or even when she copied a printed paragraph. She was extremely slow and her lips moved soundlessly as she enunciated each word to herself before writing it down.

All these tests showed that verbal formation and structure were disturbed; and she was conscious that, in spite of her great increase in power, she had not regained her normal freedom, when writing spontaneously, to dictation or to copy.

The alphabet.—All the letters were said spontaneously in perfect sequence, divided into short groups separated by a pause. She repeated them after me and read them aloud without difficulty. She could write them spontaneously or to dictation with fair accuracy, but translated capitals into cursive handwriting less easily and with several slight corrections in the shape of the letters. Given the twenty-six blocks, the order in which she placed them was correct, except that at first she placed Q for O and omitted U. This she finally discovered, but failed to find its proper place until she had repeated the whole alphabet aloud. Throughout it was evident that any difficulty she might have was with the form or shape of the letters.

A printed paragraph.—As a result of what she told me of her visit to the Zoological Gardens, I put in print the following account :—

On Sunday afternoon we went to the Zoological Gardens. We were there from 2 o'clock to 5 and had a cup of tea, when we were tired. It is an immense place and difficult to find, but we took a taxi each way. We saw lions, tigers, elephants, polar bears, a number of large reptiles and many kinds of birds. It was a beautiful afternoon and we enjoyed ourselves greatly.

This she read silently and re-told the story in the following words: "We went to the Zoological Gardens and spent an enjoyable time. We saw there elephants, tigers and various kinds of an-mals. It's a large place and diff-cult to find. We spent an enjoyable afternoon and got home about 5 o'clock in the afternoon."

When she repeated these sentences after me or read them aloud, all her faults were those of enunciation; she stumbled over many of the words, such as elephants and zoological, but finally corrected herself in most instances.

After reading the printed account through again to herself she wrote: "We went to the Zo on Sunday afternoon And spent an enjoyable treat we saw all kind of animals. We had a cup of tea Afterward we came having spent an enjoyable treat."

To dictation she wrote "On Sunday afternoon we went to the Zo gardens we were there fron two untill five and had a cup of tea when we were tired. It is an immense and difficult to find that we took a taxi each way. We saw lions tigars Elephants and polar baars and a number of large reptiles, and many kinds of birds. It was a beauliful afernoon and we enjoyed ourseilves greatly."

She copied the printed account very slowly; her lips moved and, although she uttered no sound of any kind, it was obvious that she was saying the words to herself before she put them down on paper. She wrote "On Sunday aflernoon we went to the Zoological Gardens. We were there from 2-0 o'clock to 5-0 And had a cup of tea when we were tired It is an imnense place and difficult to find. But we took a taxi each way we saw lions tigers elephants polar bears a nunber of large reptiles and many kind of birds It was a beautiful aflenmoon we enjoyd ourselves greally."

Numbers and arithmetic.—She counted correctly up to a hundred with considerable rapidity and certainty, though some of the numerals were indistinct. The order in which they were given was perfect and she did not hesitate when beginning a new decade.

Addition.	325	568	685
	432	323	737
	757	891	1422
Subtraction.	864	582	821
	432	236	348
	432	346	473

The three simple addition sums were carried out rapidly and without movement of the lips. With the second and third subtraction she said the numbers under her breath incorrectly and, recognizing they were wrong, became confused. Finally, however, she succeeded in arriving at the right answer.[1]

Coins and their relative value.— All the coins were named correctly and she was remarkably accurate in her estimation of the relative value of any two of them placed on the table before her. But she not infrequently found it difficult to arrive at the answer directly without counting up under her breath. Thus, given sixpence and half a crown, she whispered "one, two, three, four, five" and then said aloud "five" the correct answer.

She denied she had any difficulty with money and added "My speech is the worst . . . you know . . . if it wasn't for that . . . I could . . . go . . . shopping."

Orientation.—She could find her way perfectly and went about alone in her native town. I could not persuade her to produce a ground plan, because she asserted she had never been able to draw; but she could describe accurately the various pieces of furniture in my room and their relation to one another.

Serial Tests.

(1) *Naming and recognition of common objects.*—All these tests were carried out accurately and she could even write down the name of each object as it was shown to her; but her handwriting was poor and some of the letters were malformed, though no word was actually misspelt.

(2) *Naming and recognition of colours.*—She named all the colours without fail both by word of mouth and in writing, and chose them correctly to oral and printed commands.

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[1] At the beginning of our next sitting, when she was fresh, I set her the same sums, which she solved correctly at the first attempt.

(3) *The man, cat and dog tests* were executed perfectly in every respect.

(4) *The clock tests.*—She carried out oral and printed commands with considerable rapidity. The time shown on the clock was stated correctly; but, with the higher number of minutes, she tended to count up instead of giving the answer directly. Thus, shown 20 minutes to 4, she said "five, ten, fifteen, twenty to four." She had considerable difficulty in writing down the time and in every instance first enunciated in a whisper the words she ultimately wrote. This preliminary verbalization, whether right or wrong, determined what she put on to paper and she did not look back repeatedly at the clock face for guidance during the act.

The results of this test were as follows:

Time shown on the clock		She wrote
5 minutes to 2	..	5 minites to 2
Half past 1	..	½ past to 1
5 minutes past 8	..	5 past eigt
20 minutes to 4	..	5 (erasure) to 4
10 minutes past 7	..	10 past 7
20 minutes to 6	..	5.20 to 6
10 minutes to 1	..	ten minites to one
A quarter to 9	..	quarter to nine
20 minutes past 11	..	twenty past eleven
25 minutes to 3	..	five & twenty past two

Many of the words were so badly written, that it was difficult to be certain of the actual letters employed; thus minutes was written "mimtes" with no distinction between the up and down strokes belonging to each letter. Verbal structure was inherently faulty and calligraphy suffered.

(5) *The hand, eye and ear tests.* She had completely recovered her power of imitating movements made by me, when we sat face to face, and oral and printed commands were executed with remarkable quickness and certainty. The only errors occurred when she was asked to write down silently the movements made by me. Out of sixteen attempts she made three slight mistakes, substituting the *left* for the right ear; in every other case her written statement of the action I had performed was accurate.

Asked if she found these tests difficult, she replied "No . . . I seemed to think . . . or fancy . . . your right hand was opposite to me . . . so I put it so."

§ 2.—*A Case of Verbal Aphasia due to Gunshot Injury over the anterior portion of the Precentral Gyrus. Seven years and eight months later speech had recovered to a great extent, although it still showed characteristic signs of Defective Verbal Formulation.*

No. 6.—Private Thomas McB., aged 19, was wounded on March 12, 1915. A piece of shrapnel struck him in the left temporal region, producing a long incised wound which penetrated the skull.

He did not become unconscious and remembers everything that happened. He was carried at once to a field ambulance, where no operation was performed. "At first," he said, "I couldn't speak at all . . . say oh! . . . only oh!"

He was admitted to the London Hospital on March 16, 1915, and although he was not then under my care I was able to make a complete examination before his discharge on April 12.

The wound, a suppurating cut like that of a knife, extended for 5 cm. almost vertically on the left side of the scalp. It penetrated all the tissues including the bone, and the dura mater 'could be seen laid bare in its deepest part. The upper end was about 5·5 cm. from the middle of the scalp, and 14 cm. back from the root of the nose. It lay 0·5 in front of the interaural line, whilst its extreme lowest point extended somewhat farther forwards (3 cm. in front). The whole nasion-inion measurement was 34·5., and this was intersected at 14·5 cm. by the interaural line. This wound closed rapidly and finally healed on April 12 (cf. fig. 1, p. 395).

He was extremely bright and intelligent, amused at what went on around him and in no way emotional. He responded rapidly and well to commands.

He used his right hand in the normal manner and, on recovering his speech, asserted that he had always been strongly right-handed.

There were no convulsions or seizures and, although he suffered from a good deal of headache when first admitted, this passed away rapidly.

Vision was 5/15 in both the right and left eyes; but owing to his loss of speech this was difficult to test. The visual fields were in every way normal on perimetric examination. Hearing, smell and taste were intact.

The pupils reacted well and the eyes moved perfectly in all directions. The only abnormal signs were slightly defective movement of the lower half of the face on the right side and some deviation of the tongue to the right.

All the reflexes, including the abdominals and plantars, gave a normal response.

There was no paralysis, paresis, inco-ordination or difference in tone of the limbs on the two sides of the body.

Sensation was completely unaffected when tested within three weeks of the injury (April 7). During these tests he showed his remarkable intelligence. When weights of 100 and 80 grm. were placed in succession on his right palm or fingers, he indicated correctly and without hesitation which was the heavier. Sometimes he said "erst" (first) or "hend" (second). If the heavier weight followed the lighter, he usually nodded his head and said "is" (this), Tested with the compass-points he said "won" (one) and a guttural explosive sound, which I came to recognize as signifying two. Throughout the whole series he did not make a single mistake with the points at a distance of 1 cm. from one another. He was equally accurate with vibration, showing that no form of discriminative sensibility was affected.

Condition of Symbolic Formulation and Expression between March 16 and April 12, 1915.

At first he was speechless and silent, but shortly after his admission to the hospital he began to make articulate noises, which seemed to bear no obvious relation to the words he was striving to pronounce. Asked his name he said "Hō-nus," and told to repeat it after me, he again produced the same sound.

When a question put to him required an affirmative reply, he nodded, saying, "ep" or "ons"; on the other hand, to signify a negative he shook his head and uttered a nasal sound "ong," which closely approached a gutteral rendering of "no."

His power of finding words rapidly improved, and less than a month after the date of the wound he could say the alphabet and days of the week, although both letters and words were extremely badly pronounced. An attempt to say the months of the year led to a series of incomprehensible sounds. When he repeated the alphabet, the days of the week, or the months, his pronunciation was equally defective.

He undoubtedly understood what was said to him, and commands demanding a single choice were carried out accurately. Thus, he had no difficulty in putting out his tongue, shutting his eyes, or giving his hand, when asked to do so. But, as soon as two of these orders were combined, his response became slow and hesitating, and he was liable to fall into error.

Command	Movement executed
(1) Give me your hand and put out your tongue	Correct
(2) Shut your eyes and put out your tongue	Correct, but also gave the hand
(3) Put out your tongue and give me your hand	Correct
(4) Give me your hand and shut your eyes	Correct, but he opened his mouth though he did not protrude his tongue
(5) Shut your eyes and put out your tongue	Correct
(6) Give me your hand and shut your eyes..	Correct
(7) Put out your tongue and give me your hand	Correct
(8) Give me your hand and put out your tongue	Correct
(9) Give me your hand and shut your eyes..	Correct; but lips were also parted
(10) Shut your eyes and put out your tongue	Correct
(11) Give me your hand and put out your tongue	Correct
(12) Put out your tongue and give me your hand	Correct
(13) Give me your hand and put out your tongue	Correct
(14) Give me your hand and shut your eyes	Correct; but lips were also parted
(15) Put out your tongue and give me your hand	Correct
(16) Shut your eyes and put out your tongue	Correct

He could whistle perfectly any melody he happened to know, and sang "Tipperary" without the words in excellent time and tune. The musical phrases were superposed on many different articulated sounds, none of which were words; they consisted of various combinations of vowels and consonants, which might have been taken for words imperfectly heard.

Given a newspaper, he seemed as if he could read it, but his comprehension of printed phrases was obviously defective. He could reproduce accurately in writing the simple words of the man, cat and dog tests, after reading them silently, although the card was removed from his sight.

He could write his name and address correctly as "Thomas McBain, 44, Constable Street, Dundee"; but he directed a letter to his mother:

"Mrs. McBain, 44, Conbbse Street, Duddee." He failed to write the same words correctly, if they were started in a less automatic manner.

I seated him at the window and asked him to write down what he saw, and he produced the following list: Barrows, cars, shops, folowers (flowers), loan-office, artillery, four." The "loan-office" was a pawnbroker's shop, over which was the inscription "goldsmith and silversmith" and the usual three golden balls. Then some soldiers went by carrying their equipment; I asked how he knew they were artillery, and he pointed to his head in the position of the badge upon a military cap. "Four" was written as a funeral went by; but he could not explain himself further in writing, shook his head and gave up entirely.

Simple phrases were written badly to dictation, and he frequently failed to finish the sentence. He did not write wrong words; it was their formation that was faulty. He could, however, transcribe print into cursive handwriting.

Asked to count aloud, he began: "Ong, nud, ed, hon," and then stopped; but taking a pencil with his hand he rapidly wrote all the numbers up to 21 correctly.

He was particularly good at drawing, both spontaneously and to command. Asked to name the geometrical figures, he drew them rapidly, and occasionally appended some word such as "square," "ovel," or "marble," to represent the cube, ovoid and sphere.

He had no difficulty in finding his way, and there was no reason to suspect any defect of orientation.

Condition in October, 1915, *Five Months after the Injury.*

He was in excellent general health. The wound was a longitudinal painless scar with a deep fissure in the centre extending through the skull. No pulsation could be felt, and he did not suffer from headache or other local symptoms. There were no abnormal physical signs; even the lagging of the lower half of face on the right side and the slight deviation of the tongue had passed away.

He was extremely bright and intelligent. He could give a good account of what he wanted to express, in spite of his defective speech, and I was able to carry out a more exacting series of tests than was possible during the acute and severe stage of his disorder.

Articulated speech.—He talked slowly, and had evident difficulty in forming his words. The phrases, and even the longer words, were split up into groups of syllables separated by pauses. He explained to me as follows the meaning of a picture selected from one of the illustrated papers: "It's the . . . North . . . ụm-land . . . Fūs-leers . . . fighting fifth . . . met attack . . . on their first line of trenches" (How the Northumberland Fusiliers, the Fighting Fifth, met an attack on their first line trenches). In attempting to describe his condition on first entering the hospital he said: "When I come . . . I knew what you said . . . wanted answer back . . . knew what . . . couldn't get spēshe right."

He did not employ wrong words, and his power of naming was perfectly preserved, although verbal structure was defective.

He did not change the content or significance of words or phrases he was asked to repeat; the words, however, were badly pronounced.

Understanding of spoken words.—He could understand all that was said to him, selecting common objects and setting the clock correctly to oral commands. He was also able to carry out the hand, eye, and ear tests slowly, but without mistakes, when the order was given in spoken words.

Reading.—He undoubtedly understood what he read silently and gave an excellent account of the information conveyed in a paragraph chosen from the newspaper. He selected the following: "The period of grace given to Bulgaria by Russia in her ultimatum requiring Bulgaria to break with Germany and dismiss her German officers appears to have expired, but no reply had become known late last evening. In the meantime the Allies' proposals to hold a portion of Greek and Serbian Macedonia in trust for Bulgaria have lapsed as no answer has been returned to them." After reading this through to himself he said: "There was a message . . . sent from Russia to Bulgaria . . . to clear . . . out . . . all the German officers . . . art their country . . . They've got no response . . . to their message . . . so it means . . . the claration of war by the ollies."

Writing.—He now wrote well but the form of the words tended to show the same faults as those of external speech. Thus, the months written spontaneously became "Junuray, Febury, March, april, june, July, august, september, Otuober, november, december.

He could write down the movements I made when sitting opposite to him, although he complained that "It takes a lot of thinking."

Asked to write down the meaning of the passage he had read to himself (*vide supra*) on the ultimatum to Bulgaria, he produced the following account: "Russia sent a message to Bulgaria telling them to clear out all the german Officers out their country, but they got no response to their message, so that means the declaration of war by the Allies."

The same paragraph was then dictated and he wrote as follows, very slowly and with great effort: "the period of grace given to Bulgari by Russia in her altimatum requiring Bulgaria to break with Germany, and dismiss her German Officers apperes to have expired but no reply had become known leate last evening." He made several corrections which were all in the right direction.

The alphabet.—Asked to say the alphabet, many of the letters, though recognizable, were grossly mispronounced. The first half was given in the correct order but he ended: "p q e u s t v double v x y and z." He said, "I don't know whether n comes before them" (the m), although he had placed it correctly.

He wrote the alphabet spontaneously in the following sequence, sometimes in capitals and sometimes in small cursive letters. "A b C d E F G H I J k l n m o p Q u r s t v w x y z."

He was then given block letters and told to construct an alphabet from them. He quickly put together the first eleven in sequence and continued "L N M O P Q W V W"; he then removed V W, replacing them by "R S T," so that the sequence ran "P Q U R S T V W Z Y." After pondering over this for a time and shifting the last four letters, he produced "A B C D E F G H I J K L N M O P Q U R S T V W X Y Z."

Thus obviously more than articulation was at fault in this case. Internal verbalization, necessary for the production of a perfect alphabetical series, had also suffered; and indeed, when asked to think of the alphabet, most persons say the letters to themselves silently.

Arithmetic.—He was an intelligent young Scotchman, who told me he had reached the fifth standard at 13 years of age, and said "I was . . . pretty good . . . sums." But he failed to solve correctly the third addition and all the subtraction sums.

Addition.

123	..	356	..	287
243	..	235	..	376
366	..	591	..	653

Subtraction.

568	..	862	..	621
234	..	546	..	258
302	..	311	..	313

Games.—He played an excellent game of dominoes and corrected me when I was wrong; he never hesitated or made a mistake.

Serial Tests.

(1) *Naming and recognition of common objects.*—He had no difficulty in pointing to the object shown to him, named orally and in print, or placed in his hand out of sight. Asked to give their names he answered slowly but correctly although the words were poorly pronounced; he complained: "That's very slow, though I can make people understand what I mean." Each word could be repeated, but here his articulation showed the same kind of faults as voluntary speech. Told to write the names, as each object was shown to him, he wrote as follows: "knife, key, pincile, sissiors, matches, penny, sissiors, key, knife, penny, matches, pincile, sissiors, matches, key, pincile, knife, penny." He added: "How is it about scissors? . . . Only time I write . . . write home . . . very difficult . . . still gittin better . . . every day."

(2) *Naming and recognition of colours.*—He chose the colour shown to him, named orally, or in print, without the slightest difficulty. Told to name the colours one by one, his nomenclature was perfect, but violet was liable to be called "voilet" and orange "orage." Except "voilet" they were written correctly, but very slowly. He explained "Slow in writing . . . I think I'm right . . . In Lon-on Hospedl I couldn't spell . . . my own name." This alludes to his previous stay in the hospital, when his power of writing was very defective.

TABLE I.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Pictorial commands	Pictorial commands reflected in a mirror	Oral commands	Printed commands (silently)	Reading aloud and executing printed commands		Writing down movements made by the observer
							He said	Movements executed	
L. hand to L. ear..	Correct	Correct	Slow, correct	Correct	Correct	Correct	Correct	Correct	Correct
R. hand to R. eye..	,,	,,	L. hand to L. eye	,,	,,	,,	,,	,,	,,
L. hand to R. ear..	R. hand; then correct	,,	Correct	,,	,,	,,	,,	,,	L. hand to R. *eye*
R. hand to R. ear..	Correct	,,	,,	,,	,,	R. hand to L. ear	,,	,,	Correct
R. hand to L. eye..	,,	,,	,,	,,	,,	Slow; correct	,,	,,	,,
L. hand to R. eye..	R. hand; then correct	,,	,,	,,	,,	R. hand; then correct	,,	,,	,,
R. hand to L. ear..	Correct	,,	,,	,,	,,	Correct	,,	,,	,,
L. hand to L. eye..	R. hand to R. eye	,,	R. hand; then correct	,,	,,	L. hand to R. eye; then correct	,,	,,	,,
L. hand to R. ear..	Correct	,,	Correct	,,	,,	Correct	,,	,,	,,
R. hand to L. eye..	,,	,,	,,	,,	,,	,,	,,	,,	Very slow, correct
L. hand to L. ear..	,,	,,	,,	,,	,,	Slow, correct	,,	,,	Correct
R. hand to R. eye..	,,	,,	R. hand to R. *ear*	,,	,,	R. hand to L. eye	,,	,,	,,
R. hand to L. ear..	,,	,,	Correct	,,	,,	Correct	,,	,,	,,
L. hand to R. ear..	,,	,,	L. hand to R. *eye*	,,	,,	,,	,,	,,	,,
L. hand to R. eye..	R. hand; then correct	,,	Correct	,,	,,	,,	,,	,,	,,

(3) *The man, cat and dog test.*—He could read these sentences aloud from print, and both read and wrote correctly from pictures. He reproduced the different phrases exactly to dictation, and throughout these tests showed no hesitation. The difficulty was solely one of pronunciation.

(4) *The clock tests.*—He had no difficulty in setting the hands in imitation and to oral or printed commands. He told the time slowly but correctly, pausing between each word. Many were badly pronounced; he spoke of "er-levn" (eleven), minutes became "mints," but he always employed the common nomenclature. When he wrote down the time, without saying it aloud, he made one mistake, which he ultimately corrected after two attempts; he wrote first 20 to 2 (for 8.20), then 20 to 8 and finally said, "That's wrong, ten past eight." He usually wrote in numbers, but never used railway time. He had evident difficulty in retaining the words in his memory and repeatedly looked back at the clock during the act of writing.

(5) *The hand, eye and ear tests.* (See Table I.)

When he attempted to imitate my movements sitting face to face, or when carrying out pictorial commands, he made several errors; but as soon as either my hands or the pictures were reflected in the mirror, he had not a moment's hesitation in performing the desired actions correctly. He said, "Do 'em right . . . you at back of me." He was somewhat slower in executing oral commands and made several errors in answer to printed phrases read silently. But, when he was permitted to say them aloud, all his answers became correct and he explained "All the time I'm telling myself what to do." He wrote down my movements sitting face to face with one mistake only; but he said "It takes a lot of thinking."

On the conclusion of these tests he explained, "I do the think . . . I think about it . . . after-wds . . . to see right or wrong . . . often try to make it right . . . it's gone . . . most cases . . . Afterwards . . . when I think about the thing . . . I've got to spell the word . . . every letter.

Condition in November, 1922, *Seven Years and Eight Months after he was wounded.*

The wound was represented by a firm scar running somewhat obliquely upwards in the left temporal region; the opening in the bone, just over 3 cm. in length and 0·75 cm. in breadth, formed a long gutter-shaped slit, exactly as if it had been cut away with a gouge. It did not pulsate, and throughout the period of five days during which he was under observation the scalp was not tender and he was free from headache. He could lift bales of cotton and stoop to do up his boots without discomfort; but violent changes in posture, and the intellectual effort of reading, were liable to produce pain over the forehead, particularly on the left side, associated with tenderness in the neighbourhood of the wound.

He had not suffered from any form of fits or seizures and was free from nausea or vomiting. On examination I could find no signs whatever pointing to any abnormality in the central nervous system. Face and tongue moved well, the reflexes were normal and there was no paresis, or affection of even the highest forms of sensibility.

His general condition was excellent and he was in full work as an unskilled labourer. His intelligence was extremely good; willing and anxious to help, he was easy to examine and his answers often showed remarkable powers of introspection.

Communication with his fellows was hampered by his difficulties of speech and this tended to make him reticent, except with those who took the trouble to understand him. On this he laid great stress; for, when people did not grasp what he said, he was liable to become confused. "It seems this has left me more simple-like than I should be . . . There seems to be some weak part about me that I can't understand . . . I don't seem to be like the other men . . . I can't seem to go and be hearty . . . I go quietly . . . I enjoy myself, when I go quietly."

Articulated speech.—He talked slowly and with obvious difficulty; the words, especially the longer ones, were badly formed. When he pronounced a word badly, he went back over it again, recognizing that it was wrong; but his efforts to correct it frequently ended in confusion. He did not omit or seek to avoid some difficult word required to express his thoughts, but made an attempt to employ it and, if he failed, would try until he either succeeded or became confused. He spoke in a sing-song manner, breaking up his sentences into short blocks of words; but their grammatical sequence was usually perfect and he showed no tendency to omit conjunctions, prepositions and articles. For instance, "My mother says . . . I moan terribly . . . when I sleep." The rhythm was, however, disturbed, because his phrases were broken up into abnormally short groups of words in consequence of difficulty in verbal expression.

He repeated accurately single words, such as the names of familiar objects, colours, or the days of the week, and found no difficulty with the simple phrases of the man, cat and dog tests. But articulation and rhythm were affected in exactly the same manner as with voluntary speech, though to a somewhat less degree.

Understanding of spoken words.—There could not be the slightest doubt that he comprehended the meaning of simple language. Thus he said, "I quite understand what they say. . . . It's difficult sometimes. . . . I can't exactly explain. . . . At home . . . on important business. . . . I always have someone with me. . . . They don't understand me . . . I don't understand them if they speak too quick for my thinking. . . . It's quite alright if one understands you . . . but if I've got to explain my position . . . I'm fixed."

Orders given by word of mouth, even the complex hand, eye and ear tests, were quickly and accurately executed.

Reading.—He read little to himself and, when I asked for the reason, replied, "I've no desire to . . . I need to read the same thing over twice . . . before I could explain . . . what I've been reading about." All printed commands were, however, carried out perfectly.

Writing.—He could now write an excellent letter, provided he was allowed "plenty of time." The only mistakes appeared as occasional doubt with regard to the position of the letters in some word, often of the simplest character.

The alphabet.—In spite of the fact that his only faults appeared to be articulatory, he failed to say the alphabet spontaneously. He gave the letters correctly up to l, then paused and continued, "n m o p q v . . . wrong there . . . q r s t e w x y z."

He repeated the whole series correctly after me and read them somewhat slowly from print, adding, "It's the Q's and U's I get mixed up."

Asked to write the alphabet, he produced with obvious difficulty an accurate sequence up to p; then he continued, "q u v w x y z." On a second attempt he wrote "q u r s t v w x y z," adding "That's hard." All the letters were written perfectly to dictation; but, when transcribing capitals into cursive script, he made two mistakes, which he finally corrected.

Given the twenty-six block letters he had difficulty in recognizing the A because it was upside down: I reversed it and he at once started to put together A B C D E F G (upside down) H I J K L M N O P R S T U V W X Y. He then discovered the Q, and, after much hesitation, placed it correctly and added the Z. This, he said, was easier than writing, "because of course there is no spelling attached to it. . . . Q's and U's mostly get mixed up."

A printed paragraph.—I used for this series of tests the following short account of his own history: "I was a private in the 4th Battalion of the Black Watch, Royal Highlanders. I was trained in Dudup Castle, and went to France in February, 1915. Nineteen days later I was wounded by the explosion of a shrapnel shell. Within a few days after being wounded I was taken to the London Hospital."

This he read silently and when asked what he had gathered, replied, "I've been a private in the 4th Black Watch and training at Dudup Castle. I went to France in 1915. I was wounded by the explosion of a shell nineteen days later. I was taken to the London Hospital. I don't forget that."

After again reading the paragraph through silently, he wrote, "I was a privat in the 4th Battalion royal highlanders and trained at Dudup castle. I went to France in February 1915 I was wounded, in a few days later I was taken to London Hospital." Then he said, "I've missed out some word, I think. . . . I was wounded by the explosion of a shell . . . shap . . shapnal. . . . That's what I left out."

He read three sentences aloud from print as follows: "I was a private in the fourth Be-taln of the Black Watch, Royal Highlanders . . . I was train in Dudup Castle, Dundee and went to France . . . in Feb-ūrie . . . 1915 . . . Nineteen days later . . . I was wounded by an explosion of . . . a sher-ap-nel shell . . . Within a few days after . . . being wounded . . . I was taken to the London Ors-pedl." He added "The words . . . seem to . . . stand still . . . I can't go further . . . as if I were in a deep thought . . . When I'm like that . . . I have to draw away my head from the print and look back again . . . By that time I may have lost my place . . . and have to start over again."

To dictation he wrote : "I was a privite in the 4th. Battalion of the Black Watch Royal Highlanders. I was trained in Dudup Castle Dundee and went to France in Feburary 1915 ninteen later I wounded by the expload of a s shell within a few days after being wounded I was taken to the London hospital." Then he wrote spontaneously in amplification of the sentence where he had failed, "ninten days later I was wounded by the esplocdion of a — shrapnel."

He then copied the whole paragraph correctly from print, adding, "That's a great piece of work for me doctor . . . It's the forgetting . . . I know what's to be done . . . and yet I can't do it . . . Just the same as your speaking to me . . . I understand what you say . . . but later on I would forget . . . quite a lot that you would be speaking about . . . I don't forget what I'm . . . talking about . . . It seems that words that are spoken . . . have a better impression . . . on my mind."

Finally I asked him to tell me what it was all about, and he replied, "About being a private in the Black Watch . . . and being nineteen days in France . . . I'm trained at Dudup Castle, Dundee . . . nineteen days in France . . . I was wounded . . . a few days after being wounded I was taken to the London Hospital . . . wounded by explosion of a shell . . . a shar-a-nel shell. I quite remember in France what I did . . . and then I don't remember any more . . . I knew the pre-dick-ment (predicament) I was in . . . I saw the flare of the shell . . . and I felt the burning sensation in my head . . . When I tried to speak . . . I'd no speech . . . The right thumb was dead . . . I couldn't feel with it for about three days."

Numbers and arithmetic.—He counted slowly and deliberately without mistakes up to 100. Articulation was somewhat slurred, especially when he came to the seventies ; he said "Seven-y-one" instead of seventy-one and "hun-dert two" for a hundred and two. All the numbers were written in sequence without error of any kind.

Given the following exercises in simple arithmetic, he failed to solve the last subtraction sum, saying, in conclusion, "The diff-ulty . . . I can hardly explain . . . it's the thinking . . . a kind of . . . hesitation . . . If I'd be getting plenty of time to do it . . . I'd be doing it perfectly . . . The num-mers (numbers) . . . you see I must move my lips . . . I had to say . . . different figures . . and different methods . . . I must find the smallest of the words . . . because I can't speak much."

Addition.

123	..	356	..	287
243	..	235	..	376
366	..	591	..	663

Subtraction.

568	..	862	..	621
234	..	546	..	258
334	..	316 (Corrected)		263

Coins and their relative value.—All the pieces of money from a halfpenny to a pound note were named accurately, and their relative value was explained with ease. He experienced no difficulty with change and managed his money affairs with considerable ability; thus, he took his own ticket from Scotland with the money I sent him, and gave me an exact statement of his expenditure.

Drawing.—He had no difficulty in drawing either from a model or from memory. He produced an excellent outline of an elephant, naming each salient part correctly as he filled it in.

Orientation and a ground-plan.—He found his way with ease even in London, and was entirely free from confusion with regard to the objects in a familiar room. He drew an excellent ground plan saying, "I just imagined . . . for a moment . . . I was in that room . . . I could see the room." I then asked, "Can you see the colour of the things in the room?" He replied, "The cupboards are white . . . the table where we were sitting was square . . . it was brown;" all of which statements were correct.

Games.—He played a good game of draughts and was fond of cards; but he added, "I play in the slow style . . . I've got to think."

Serial Tests.

(1) *Naming and recognition of common objects* was performed accurately, but he said, "If I didn't pay strict attention I'd be wrong." All the names were written correctly except scissors, which became "cissors" or "sissors," and he complained "That's the diff-ult (difficult) one." To dictation the words were somewhat better written, and he copied them correctly from print.

(2) He named and recognized *colours* perfectly, and carried out—

(3) The *man, cat, and dog tests* without difficulty.

(4) The *clock* was set to oral or printed commands given either in the usual nomenclature or in railway time, and he told the time correctly, though his articulation was somewhat defective; thus, five minutes past eight became "Fi min-uts pass eight," though in every case the hour was given without hesitation. Asked to write down the time, he found great difficulty in spelling minutes (written "munites," "ninutes," or sometimes correctly); but the hour was never in doubt.

(5) All the *hand, eye and ear* tests were now executed correctly. To oral and printed commands the movements were made with quickness and precision, but imitation face to face was carried out more slowly, and when executing pictorial orders he corrected himself on several occasions. He showed remarkable accuracy in writing down movements made by me, although he was slow and deliberate.

§ 3.—*A Case of Syntactical Aphasia, due to Perforation of the left Temporal Lobe by a Rifle Bullet. Typical "Jargon" and other signs of injury to this region, such as Quadrantic Hemianopia and Epileptiform Attacks, preceded by an Aura of Smell.*

No. 15.—Private Edward S., aged 25, was admitted to the London Hospital on March 2, 1915, with a gunshot wound of the head. He was incapable of giving any account of his injury, and the sole information sent with him, was a card stating that he was "admitted to No. 2 Stationary Hospital on February 2, 1915, with an operation wound of the head" and that "mentally he has improved steadily since admission; no further operation performed."

A rifle bullet had entered just to the left of the inner canthus of the right eye, and had made its exit directly above the insertion of the left ear. The wound of entry was represented by a minute perfectly healed white scar. On the other hand its exit consisted of an irregular opening in the bone and tissues of the scalp, and through this protruded a small suppurating hernia cerebri, which pulsated. Bone had been removed over an irregularly quadrilateral area about 3 cm. in vertical and the same distance in horizontal extent; below, this opening reached the level of the insertion of the ear, and above it was about 13 cm. from the middle line of the scalp. The nasion-inion measured 35 cm., and the anterior border of loss of bone corresponded to a point 13 cm. along this line, whilst the posterior edge was 3 cm. behind it. Above the wound was a large horseshoe-shaped surgical incision, which had healed completely. (Cf. figs. 2 and 3, pp. 398 and 400.)

He did not as a rule say anything spontaneously; but in answer to questions his speech was jargon. When he wanted to ask if he might smoke, he said, "Want treat Christian;" but the intended meaning of the words became obvious, when he put an imaginary cigarette into his mouth and pretended to light it.

The left pupil was fixed and the cornea insensitive; the lid drooped and he was unable to move the globe in any direction except downwards. This eye was blind from rupture of the choroid and atrophy of the optic nerve. Evidently the bullet had caused gross damage to the left eye as it passed backwards in the direction of the temporal lobe.

The lower portion of the right half of the face moved slightly less than the left, and the tongue was protruded a little to the right of the middle line. Arm-jerks and knee-jerks were brisker on the right than on the left side and there was a tendency to clonus at the right ankle-joint. The right plantar reflex gave an upward response, whilst the left was normal. Over the left half of the abdomen the responses were unaffected; but on the right side no reflex could be obtained from the lower segment, whilst that from the upper part of the abdomen was evidently diminished. Motor power, muscular tone and co-ordination were unaffected and sensation appeared to be normal.

Condition in June, 1915, eighteen weeks after he was wounded.

By June 5, 1915, the cerebral hernia had entirely disappeared, the wound was firmly healed and he was up all day, busy and helpful in the ward. During the following week a complete series of observations was made with the following result.

He had suffered from no fits or seizures during his stay in Hospital, and was free from headache and vomiting. The left globe was shrunken and had subsequently to be removed. Vision of the right eye was $\frac{6}{6}$, but there seemed to be some restriction of the upper part of the outer quadrant of the visual field, although the right fundus showed no definite changes. He was somewhat deaf in the left ear, but he thought that the tuning-fork placed on the forehead was heard better on this side. No gross changes could be seen on otoscopic examination, though apparently the bullet on making its exit had in some way injured the auditory apparatus of the left ear. Smell and taste were certainly unaffected. There was still a little weakness of the lower portion of the right half of the face, and the tongue was protruded slightly to the right of the middle line. Arm-, knee- and ankle-jerks were brisker on the right side than on the left, but there was no ankle clonus. The right plantar reflex gave an upward response, whilst the left great toe went downwards. The lower segment of the right half of the abdomen now responded to stimulation, but the reflex was diminished and was less than that obtained from any other portion. There was no paralysis or paresis and sensation was not affected.

Symbolic Formulation and Expression.

He was cheerful and willing, laughed when he was successful in performing the task set him, and did not become irritable, though he failed to express himself intelligibly. When he recognized that his jargon was incomprehensible, he dropped his head and sometimes showed the beginning of a blush; he did not then care to make another attempt to express those particular thoughts. He was intelligent and useful in the work of the ward, provided he was not compelled to express himself in speech. For example, he would go about serving the patients, washing up, laying the cloth correctly; but as soon as he attempted to formulate his wants, such as that he required a purge, he became confused, not only in utterance but in thought.

Articulated speech.—He said little spontaneously, but answered questions readily; once started, his speech was rapid and voluble. He tried to "rush" his phrases and not uncommonly was brought to a standstill by pure jargon. It was extremely difficult to hear the prepositions, conjunctions or articles, and these parts of speech were frequently omitted. Thus, asked what he had done since he came to the London Hospital, he said "To here; only washing; cups and plates." Q. "Have you played any games?" A. "Played games, yes, played one, daytime, garden." Q. "What did you play?" A. "We had four bowls each; big bowls; about four each. Always chuck to a small white 'un; try to hit it. Round one, flat one; chuck it on to flat bit of wood. Me and another try to play it, see who could get the most, numbers." Asked about his wound he said, "When I woke straight in bed; I couldn't say it. I knew what it was, but couldn't say it. I couldn't say, France nobody was; but I couldn't say it."

He did not use wrong words, and if the subject under discussion was known, it was not difficult to gather the sense of what he said. Thus, when I was testing his taste, and placed some quinine upon his tongue, he said: "Rotten to drink it. Something medicine or that. Make you drop of water after it, so to take out of your mouth." The rhythm of the words and the balance of each phrase was mainly affected. Syntax was gravely disordered.

He could say the alphabet and the months correctly and in order.

Understanding of spoken words.—He seemed to comprehend what was said to him, and carried out simple oral commands correctly; thus he chose without fail a common object or colour named by me. But, as soon as the order of necessity took the form of a group of words or a short phrase, it was executed more slowly and with some hesitation; when setting the hands of a clock, he was liable to confuse "to" and "past" the hour, and he made several mistakes with the hand, eye, and ear tests.

Reading.—He was asked to select something from the daily paper to read aloud, and chose the following large block type heading on the front page: "Mr. Lloyd George says Red Tape must go. The Truth about Przemysl. Russians evacuate Galician town after removing guns and stores. Success in the North. German lines pierced and prisoners taken." These he read rapidly as: "Mr. Lloyd George says red take, take must go. The troop about towns, what lost 'em. Russ-ns exclose some big town after refunded . . . re . . . refunded guns and stories . . . stoppies. Success in the north. German binds prisoners and prisoners taken."

I then said: "You have just read me something; what was it about?" He answered: "What looking at paper?" "Yes." He then continued: "Germans what lost big town and the Americans . . . Germans have already won it. Some of the prisoners on its road, its country . . . prisoners, over it. Mr. Lloyd George says, Act beer something." The substitution of "Red take must go" for "Red tape," when he read the readings aloud, evidently confused him, and, on attempting to reproduce the meaning, he substituted legislation about beer, much discussed at this time.

He chose a common object or colour, and set the hands of a clock quickly and accurately to printed commands; but he carried out the hand, eye, and ear tests slowly and with several errors. So long as the order was given in a single word, his response was prompt; on the other hand, a phrase, which he was compelled to repeat to himself silently before he performed the movement required, was liable to lead to confusion.

He understood not only the details but also the general meaning of pictures, though he had extreme difficulty in formulating aloud what he had learnt from them.

Shown a picture of two Belgian gunners explaining the mechanism of a field-gun to a British Red Cross woman worker at the Front, he said: "It's the ladies . . . come on the hospital . . . come to see how men work it." Q. "What sort of men are they?" A. "Till France . . . the men come from France . . . the France men . . . she might come from

England . . . lady." Q. "What are they showing her?" A. "A gun . . . a 75 isn't it?"

He was then told to read the legend aloud, which he did as follows: "Belgian gunners explode . . . no, explay . . . the max-stick something . . . of their wetton . . . to a Red Cross . . . worker, worker . . . She belongs to the British nursing . . some corps" (Belgian gunners explaining the mechanism of their weapon to a Red Cross worker. She belongs to a British Nursing Yeomanry Corps.)

I then asked: "What is the picture now?" and he answered: "It's a guns belongs to Belgian. . . She a hospital lady from England . . . comes from England. . . The Belgians just telling what it's made of . . . the different names, the works and . . ."

Writing.—Asked to write his name and address, he did so rapidly as Frank Edwe Sams, 203 Parkhurst Road, Manor Park, E.; but when he attempted to do the same for his mother with whom he lived, he failed entirely. I said to him: "Now write your mother's address"; he hesitated and asked: "What, her name before?" To this I replied: "No, her name now; as if you were going to direct a letter to her." He wrote "S",; then after a pause: "Sams," and, saying "Susie," gave up the attempt. Urged to try again, he wrote "S. Sams 203," and said: "No, I can't, you mean her address? No, I can't."

In response to a request to write a letter, he produced the following: "My dear Sister I now write to you that I hame getting the best of hearl, and I am getting to walk to the garden to play a lot of game and I hame the all of." Asked to read aloud what he had written he said: "My dear Sister I now write to you that I am now getting the best of health, and I getting to walk to the garden to play a lot of games, and I have the whole of . . . I've forgotten now what I was going to say."

He spent much of his time on the balcony reading the newspaper and I asked him to choose some passage, which was of interest, and to write down for me what it conveyed to him; for he told me he liked reading, "but I can't say it." The result was as follows: "the men of the rich we have been fiching for a day and we have gorn 200 yard of and we will go a . . ." I then inquired "what did you want to write?" and he answered "our division was firing . . . was firing all day . . . was fighting all day and all the regiment . . . all the regiment had moved . . . at night all the regiment moved on . . . two hundred yards all our regiment."

The alphabet was written as follows: a b c d e f g h i j k l m n o p u r s t[1] u y w x y z and when dictated a b c d e f g h i j k l m n o P Q R S T U X W Z Y Z.

Numbers and coins.—He named every coin correctly throughout a series of twenty-one tests, and had no difficulty in expressing the relative value of any two of them to one another. Simple addition and subtraction were carried out perfectly. The coin-bowl test evidently presented no difficulty and the various movements were executed without mistake both to oral and printed commands.

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[1] Probably an uncrossed t.

Drawing and pictures.—Asked to draw a spirit-lamp placed before him on the table, he produced an excellent picture and said, "I was good drawder . . . drawer . . . at school." The model was removed and ten minutes later he was asked to draw it from memory; the result was an almost exact reproduction.

Then I said to him "Draw me an elephant." He replied, "Yes I seen them . . . up other end . . . India." He then produced the following figure: (fig. 9).

When drawing (*a*) he said "mouth" and then uttering the words "irons," "highons," he added to the picture what were evidently intended for horns. After he had finished I asked, "What has an elephant got in front?" He answered, "They carry big trees . . . tied round a bit of an iron thing." I then said, "Behind you have given him a tail, what has he in front?" He replied, "He has a big one, quite straight, about a yard long." Q. "What is it called?" A. "Same what you drive water with." Q. "Has your elephant got a trunk?" A. "He's lost it" and at once he wanted to add the missing part. I then pointed to the horns he had drawn on the head of his figure, asking, "Has an elephant got horns?" He replied, "Yes silver what you stick out" (pointing to the corner of his mouth and placing his pencil into the position of a tusk). Q. "What are they made of?" A. "Kind of a white bone one, what grows in the mouth, on the roof, on the edge of the mouth." Evidently he had been confused by saying the jargon words representing horns, and

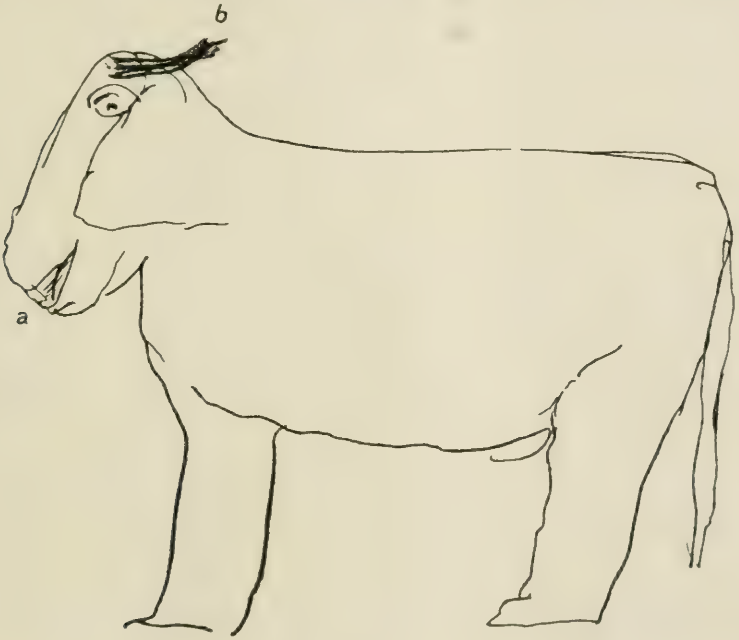

FIG. 9.

impulsively added them to the figure; but he was finally able to explain his error by gestures, giving a correct interpretation of his intention.

Games.—He played a perfect game of dominoes and was excellent at bowls.

Serial tests.

(1) *Naming and recognition of common objects.*—All these tests were carried out correctly, but on two occasions he called a pencil "black lead" or "blacking"; otherwise his nomenclature was accurate, and he was quick in selecting the object named orally or in print.

(2) *Naming and recognition of colours* :—

TABLE I.

	Pointing to colour shown	Oral commands	Printed commands	Naming colours shown	
				1st series	2nd series
Black	Perfect	Perfect	Perfect	Correct	Correct
Red	,,	,,	,,	,,	,,
Orange	,,	,,	,,	Can't say it	,,
White	,,	,,	,,	Correct	,,
Green	,,	,,	,,	Gur . . green	,,
Violet	,,	,,	,,	Vilet*	Volley
Blue	,,	,,	,,	Correct	Correct
Black	,,	,,	,,	,,	,,
Red	,,	,,	,,	,,	Blue
Orange	,,	,,	,,	Slow, correct	Vilet
White	,,	,,	,,	Correct	Correct
Green	,,	,,	,,	Blue	Slow, correct
Violet	,,	,,	,,	Volley	Volley
Blue	,,	,,	,,	Correct	Correct
Black	,,	,,	,,	,,	,,
Red	,,	,,	,,	,,	,,
Orange	,,	,,	,,	Can't think of it	More like a yellow one
White	,,	,,	,,	Correct	Correct
Green	,,	,,	,,	,,	,,
Violet	,,	,,	,,	Vilet*	Bluey
Blue	,,	,,	,,	Correct	Correct

* Probably, as a Londoner, his normal pronunciation was "vilet."

Here again he chose correctly to oral or printed commands, but the names he applied were less accurate and he was specially troubled by violet and orange.

(3) *The man, cat, and dog test.* (See Table II.) :—

He read these short phrases aloud without difficulty; but wrote them down inaccurately, not infrequently reversing the order or substituting one noun for another. Exactly the same trouble occurred when he wrote to dictation. He could, however, copy these simple phrases perfectly.

(4) *The clock tests.* (See Table III.) :—

He set one clock in exact imitation of another and told the time accurately. Printed orders were well executed, but oral commands were carried out some-

TABLE II.

	Written to dictation	Copied in cursive handwriting from the printed cards[1]	Reading aloud from the printed cards and writing what he had read	
			(a) Read aloud	(b) Wrote
The dog and the cat ..	The dog and the cot	Perfect	Perfect	The dog and the cat
The man and the dog	The men of	,,	,,	The dog and the men
The cat and the man..	The cot and the men	,,	,,	The cat and the men
The dog and the man	The dog and the men	,,	,,	The dog and the men
The dog and the cat ..	The dog and the cat	,,	,,	The dog and the cat
The man and the dog	The men and the dog	,,	,,	The men and the dog
The cat and the man..	The cat and the dog	,,	,,	The men and the dog
The dog and the man	The dog and the cat	,,	,,	The men and the cat
The dog and the cat ..	The cat and the dog	,,	,,	The dog and the men
The man and the dog	The men and the dog	,,	,,	The man and the cat
The cat and the man..	The cat and the men	,,	,,	The cat and the men
The dog and the man	The dog and the men	,,	,,	The dog and the man

[1] The handwriting was much better than in tests (1) or (3).

TABLE III.

	Telling the time	Oral commands	Printed commands	Direct imitation	Writing down the time shown on a clock-face	Printed commands read aloud and executed
10 minutes past 7	Ten past seven	Correct	Quick, correct	Perfect	10 minutes past 7	Both correct
20 minutes to 6 ..	A quarter to six	,,	,, ,,	,,	20 minutes to 6	,,
10 minutes to 1 ..	Ten to one	Slow, correct	,, ,,	,,	10 minutes to 1	,,
A quarter to 9 ..	Quarter to nine	Correct	,, ,,	,,	45 to 9	,,
20 minutes to 4 ..	Twenty to four	4.20	,, ,,	,,	20 to 4	,,
5 minutes to 2 ..	Five to two	Correct	,, ,,	,,	5 to 2	,,
20 minutes to 6 ..	Twenty to six	,,	,, ,,	,,	20 to 6	,,
Half-past 2 ..	Half past two	,,	,, ,,	,,	30 past 2	,,
20 minutes past 11	Twenty past eleven	,,	,, ,,	,,	20 past 11	,,
Half-past 1 ..	Half past one	,,	,, ,,	,,	30 past 1	,,
5 minutes past 8	Five past eight	7.55	,, ,,	,,	5 past 8	,,
25 minutes to 3 ..	Twenty five to three	2.40	,, ,,	,,	25 to . . . "I forget"	,,
20 minutes past 9	A quarter to four . . . nine twenty	Correct	,, ,,	,,	20 past 9	,,
10 minutes past 8	Ten past eight	Slow, correct	,, ,,	,,	2 past 8	,,

what slowly, and in two instances he mistook "to" and "past" the hour. He could write down the time on the whole correctly although his nomenclature was peculiar. Thus a quarter to nine became "45 to 9" and ten minutes past eight was written as "2 past 8" because the long hand, standing at ten minutes past the hour, pointed to the number 2.

(5) *The hand, eye and ear tests :—*

TABLE IV.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Pictorial commands	Pictorial commands reflected in a mirror	Oral commands	Printed commands
L. hand to R. eye ..	Correct	Perfect	Correct	Perfect	R. hand to L. eye	Correct
R. hand to R. ear ..	,,	,,	,,	,,	R. hand to R. ear ; then eye	R. hand to R. *eye*
R. hand to L. eye ..	Slow, correct	,,	,,	,,	Correct	Correct
L. hand to R. ear ..	Correct	,,	,,	,,	,,	L. hand to R. *eye*
R. hand to R. eye ..	,,	,,	L. hand to R. eye	,,	R. hand slowly to R. *ear*	Correct
L. hand to L. ear ..	,,	,,	L. hand to L. eye : then ear	,,	Correct	Slow, correct
L. hand to L. eye ..	,,	,,	Correct	,,	,,	,, ,,
R. hand to L. ear ..	,,	,,	R. hand to L. eye ; then ear	,,	,,	Correct
L. hand to R. eye ..	,,	,,	Correct	,,	,,	,,
R. hand to R. ear ..	,,	,,	,,	,,	,,	Very slow, correct
R. hand to L. eye ..	,,	,,	,,	,,	,,	Correct
L. hand to R. ear ..	,,	,,	,,	,,	,,	,,
R. hand to R. eye ..	,,	,,	,,	,,	,,	,,
L. hand to L. ear ..	,,	,,	,,	,,	,,	,,
L. hand to L. eye ..	,,	,,	,,	,,	,,	L. hand ; then R. hand to L. eye.
R. hand to L. ear ..	,,	,,	,,	,,	Very slow, correct	Correct
L. hand to R. eye ..	,,	,,	,,	,,	,, ,,	,,
R. hand to R. ear ..	,,	,,	,,	,,	Correct	,,
R. hand to L. eye ..	,,	,,	,,	,,	,,	,,
L. hand to R. ear ..	,,	,,	,,	,,	,,	,,
R. hand to R. eye ..	,,	,,	,,	,,	" No, I can't "	,,
L. hand to L. ear ..	,,	,,	,,	,,	L. hand to R. car	,,
L. hand to L. eye ..	,,	,,	,,	,,	Correct	Slow, correct,
R. hand to L. ear ..	,,	,,	,,	,,	R. hand to L. *eye*	Very slow, correct

He imitated my movements, when we sat face to face, correctly, though somewhat slowly and executed pictorial commands with three slight errors only. When reflected in the mirror, these tests were carried out perfectly and without hesitation. His response to oral and printed commands was slow and in both cases he made several mistakes ; but throughout it was easier for him to execute printed orders than those given by word of mouth.

Six weeks later he was readmitted. The observations on his speech were confirmed, but the physical signs had changed for the better. There was now no weakness of the right half of the face and the tongue was protruded straight ; the reflexes were equal on the two halves of the body and both plantars gave a downward response. Motion and sensation were unaffected.

Condition in October, 1920, *five years and nine months after he was wounded.*

The scar was in perfect condition, deeply depressed and not pulsating. It was not tender and gave him no discomfort. He suffered from no headache or vomiting, but complained that occasionally a " smell of gas " came into his mouth, which turned him from his food. This was not associated with any external manifestations, and passed unnoticed by his wife and parents. He was not unconscious, even for a few moments, but he complained "Sometimes smell of gas coming out of my mouth ; taste or something. Want to be sick and can't. Nasty smell comes out of the mouth. Feel I want to be sick ; stop me eat, eat up half my dinner and can't."

The left globe had been extracted and the socket was in perfect condition. Vision of the right eye was $\frac{6}{6}$, but careful perimetric examination under favourable conditions showed that there was distinct limitation of the upper and outer portion of the visual field. The boundaries were difficult to define and seemed to shade gradually into parts where the sight was preserved. On ophthalmoscopic examination the inner half of the disc was somewhat pale, but its edges were clear, and there were no signs of optic neuritis.

Hearing of the right ear was normal, and a watch could be appreciated at a distance of 4 ft. With the left ear he said he could not hear the watch on contact, but a tuning fork was audible at about 4 in. ; when placed on the forehead it was said to be heard better in the right than in the left ear. The left membrane was somewhat withdrawn and thickened.

Symbolic Formulation and Expression.

He was married and lived on his pension ; neither he nor his wife did any work, but they spent most of their time walking about London in the parks and wherever there was anything to be seen. Mentally he was in the same state as before ; to direct examination he was an excellent subject and his answers were remarkably constant, but, when he attempted to narrate his introspective experiences, he became confused and frequently gave up trying to make himself understood.

Articulated speech.—He still talked jargon, which was usually comprehensible if the subject of conversation was known. Thus, wanting to explain to me about a hernia, which had developed since he had left the hospital, he said, "I got that rupture, after left Hospital, when dark, no lights, when airships came over. Couldn't see, smashed the wall, the house like, smashed into wall, couldn't see. Had a pain, saw doctor, pushed it to. If it should come up, press it up and use what you call 'em. When it do go up, pain inside."

He could repeat single words or even simple phrases, such as those of the man, cat and dog test, without difficulty. But, when asked to repeat short sentences, which he had not heard before, his defective syntax became evident. For example, "I have not suffered from headache lately" became "I have not suffered headache" ; "I am afraid there is going to be a coal strike" was repeated as "I afraid there is going to be a a coal strike," and "It was difficult to find your house to-day," "It's difficult to find your house again." I then asked him to repeat together the three sentences he had said, but he answered, "There is a coal strike. I can't think."

Understanding of spoken words.—He had no difficulty in choosing a common object or colour named by me, or in setting a clock to oral commands.

Even the complex hand, eye and ear tests, though slowly executed, were carried out with two mistakes only.

But there was no doubt that he occasionally failed to comprehend exactly what he was told to do in the course of general conversation. An order given in the form of a single word or short phrase led to a prompt response. But his father, who was a builder, said that it was impossible to employ him, because of his unexpected lapses of memory; thus, told to fetch a ladder, he would bring a short plank, although he seemed at first to appreciate the nature of the order. On testing him carefully this seemed to depend on want of power to reproduce exactly a phrase or sentence he had heard; so long as the order was comprised in a single word, it was performed without hesitation.

Reading.—He had no difficulty in reading single words or the various combinations of the man, cat and dog tests. But he failed badly when made to read aloud a paragraph from the newspaper (*vide infra*). He said, "It's all right these small words: thick ons can't understand 'em."

He chose a common object or colour and set the clock correctly to printed commands: single words, or small verbal groups, seemed to give him no trouble. But he carried out the hand, eye and ear tests slowly and inaccurately.

Writing.—His signature was written perfectly and he no longer had any difficulty with the name and address of his mother. Single words used as names were badly spelt and his handwriting was poor. Simple phrases, such as those of the man, cat and dog test, when dictated, were extremely well written, though he failed badly in his attempts to reproduce a series of descriptive sentences in writing (*vide infra*).

Numbers, &c.—He could count perfectly and solved correctly the six simple arithmetical problems usually set. He had no difficulty with money or with the names and relative value of coins.

Drawing and pictures.—Told to draw an elephant he produced an inadequate figure without a trunk or tusks.

I then asked him to point to the various parts of the beast and he said: "Zisis ear" (this is his ear); "Head" "Nose" (Trunk), "Legs," "Tail," "Body," "Eye," "Mouth." I said "Have you left out anything?" A. "No." Q. "From his mouth?" A. "Bonezinks" (Bone things.)

General understanding of words and pictures.—To test his power of speech, reading, writing, together with the understanding of words and pictures, he was shown a photograph of a railway station during the war, where a collecting box had been placed for flowers to be sent to the wounded. Beneath was printed the following description. "This box has been placed on the platform at Snaresbrook station as a receptacle for flowers for the wounded. Many of the passengers contribute nosegays daily from their gardens and these are sent to the Bethnal Green Infirmary." This he read silently and, on attempting to describe in writing what he had read, got no further than "Fres flours for wooded solders for sail." The passage was dictated to him and he wrote: "This box has been on the platform at s slaton at for for the wooded many of the pas . . c . . no get dail for ther and to the . . infom." He then read the legend aloud as follows, "This box has placed on the . . platform at . . can't name either . . station . . at a . . no sir . . for flowers for the wounded. Any of the . . passengers can't stand (understand) that letter . . nosegay . . daily . . for the gardens . . and these are sent . . to the Befnal Green . . Infirm." I then asked him to show me the different objects in the picture and he pointed them out saying, "Two ladies" "buying flowers," "flowers for wounded soldiers," "box" "at Bethnal Green"; then reading the words on the box "Firmry." He evidently had not comprehended exactly what he had read, and was misled by his first statement that the flowers were "for sail"; for pointing to the station master he said, "He's selling 'em.' Then he was told to copy the description and did so perfectly; but asked to narrate what he had just written he said, "Flowers for sale; selling at stations. At Bethnal Green, at Bethnal Green station."

Serial Tests.

(1) *Naming and recognition of common objects*:—

TABLE V.

	Pointing to object shown	Oral commands	Printed commands	Naming an object indicated	Writing name of object indicated	Duplicate placed in hand out of sight
Knife ..	Correct	Correct	Correct	knife	knif	Correct
Key ..	,,	,,	,,	kay	key	,,
Penny ..	,,	,,	,,	penny	Pennie	,,
Matches ..	,,	,,	,,	matches	match	,,
Scissors ..	,,	,,	,,	scissors	cissis	,,
Pencil ..	,,	,,	,,	pencil	pencle	,,
Key ..	,,	,,	,,	key	key	,,
Scissors ..	,,	,,	,,	scissors	cissis	,,
Matches ..	,,	,,	,,	masses	match	,,
Knife ..	,,	,,	,,	knife	knif	,,
Penny ..	,,	,,	,,	penny	pennie	,,
Matches ..	,,	,,	,,	matches	match	,,
Scissors ..	,,	,,	,,	scissors	sissor	,,
Pencil ..	,,	,,	,,	pencil	pencle	,,
Penny ..	,,	,,	,,	penny	pennie	,,
Knife ..	,,	,,	,,	knife	knif	,,
Key ..	,,	,,	,,	key	key	,,
Pencil ..	,,	,,	,,	pencil	pencle	,,
	Very quick					Very quick

Oral and printed commands were carried out perfectly, and he named the various objects on the table before him correctly, apart from slight errors of pronunciation. This verbal deformation, with perfect nomenclature, was still more evident when he attempted to write the name of an object shown him.

(2) *Naming and recognition of colours.* (See Table VI.):—

Oral and printed commands were accurately executed, and most of the names given to the colours were rightly pronounced. But if he attempted to write them down the words were deformed, although the nomenclature was obviously correct. Even when he was allowed to say the names aloud, he wrote them equally badly.

TABLE VI.

	Pointing to colour shown	Oral com-mands	Printed com-mands	Naming colour shown	Writing down name of colour shown	Naming colour shown and writing down the name	
						He said :	He wrote :
Black ..	Correct	Correct	Correct	Correct	Correct	Correctly	Correctly
Red ..	,,	,,	,,	,,	,,	,,	,,
Blue ..	,,	,,	,,	Bē-lue	,,	,,	,,
Green ..	,,	,,	,,	Correct	gren	,,	gren
Orange ..	,,	,,	,,	,,	orgen	,,	orgen
White ..	,,	,,	,,	,,	whit	,,	what
Violet ..	,,	,,	,,	Vilet	viren	Vilet	vorat
Yellow ..	,,	,,	,,	Yeller	dewor	Yeller	yerow
Red ..	,,	,,	,,	Correct	Correct	Correctly	Correctly
White ..	,,	,,	,,	,,	whit	,,	what
Yellow ..	,,	,,	,,	Yeller	lemon	Yeller	yerow
Blue ..	,,	,,	,,	Correct	Correct	Correctly	Correctly
Green ..	,,	,,	,,	,,	gren	,,	gren
Black ..	,,	,,	,,	,,	blak	,,	blak
Orange ..	,,	,,	,,	,,	orgen	,,	orgon
Violet ..	,,	,,	,,	Vilet	viron	vilet	vorat

(3) *The man, cat and dog tests :—*

TABLE VII.

	Reading aloud	Reading from pictures	Writing from dictation	Writing from pictures	Repeti-tion	Reading what he had written
The dog and the cat ..	Correct	Cat Dog	The dog and the cat ..	dog and cat	Correct	Correct
The man and the dog ..	,,	Man Dog	The man and th dog..	man and dog	,,	,,
The cat and the man ..	,,	Man and cat	The cat and the man	man and cat	,,	,,
The cat and the dog ..	,,	Dog and cat	The cat and th dog ..	dog and cat	,,	,,
The dog and the man ..	,,	Man and dog	The dog and the man	man and dog	,,	,,
The man and the cat ..	,,	Man and cat	The man and th cat ..	man and cat	,,	,,
The dog and the man ..	,,	Man and dog	The man and th dog..	man and dog	,,	,,
The cat and the man ..	,,	Man and cat	The cat and the mam	man and cat	,,	,,
The dog and the cat ..	,,	Dog and cat	The dog and th cat ..	dog and cat	,,	,,
The man and the dog ..	,,	Man and dog	The man and the dog	man and dog	,,	,,
The cat and the dog ..	,,	Cat and dog	The cat and the dog..	cat and dog	,,	,,
The man and the cat ..	,,	Man and cat	The man and th cat ..	man and cat	,,	,,

These simple phrases were read aloud and repeated after me correctly. But as soon as he was asked to read or write from pictures, a curious tendency to reverse the order of the two nouns became apparent. Thus shown two pictures, a cat to the left and a man to the right, be both said and wrote "man and cat." Yet this was not universal, for on the next occasion the same combination was given correctly. Reversals of this kind also occurred when the phrases were written to my dictation; it seemed as if he found difficulty in repeating the words to himself in the correct order.

(4) *The clock tests :—*

TABLE VIII.

	Direct imitation	Clock set to oral commands	Clock set to printed commands	Telling the time	Writing down the time shown on the clock
5 minutes to 2 ..	Perfect	Correct	Correct	Five to two	five to 2
Half past 1 ..	,,	,,	,,	Half past one	half past 2
5 minutes to 8 ..	,,	,,	,,	Five to eight	five to 8
20 minutes to 4 ..	,,	,,	,,	Twenty to four	20 to for
10 minutes past 7	,,	,,	,,	Ten past seven	Ten past 7
20 minutes to 6 ..	,,	,,	,,	Twenty to six	20 to six
A quarter past 12	,,	,,	,,	Quarter past twelve	1/4 past 12
10 minutes to 1 ..	,,	,,	,,	Ten to one	Ten to one
A quarter to 9 ..	,,	,,	,,	Quarter to nine	1/4 to 9
Half past 2 ..	,,	,,	,,	Half past two	half past 2
20 minutes past 11	,,	,,	,,	Twenty past 'leven	20 past 11
25 minutes to 8 ..	,,	,,	,,	Five and twenty to eight	25 to 8
A quarter past 6 ..	,,	,,	,,	Quarter past six	half past 6
25 minutes to 3 ..	,,	,,	,,	Five and twenty three	25 to 3
10 minutes past 4	,,	,,	,,	Ten past four	10 past 4

He set the clock to oral and printed commands and told the time correctly. When he attempted to write down the time shown on a clock set by me, the words were deformed, but the nomenclature was accurate.

(5) *Hand, eye and ear tests.* (See Table IX.) :—

He imitated my movements, sitting face to face, and carried out pictorial commands without mistakes of any kind; but he was much quicker and more certain when either of these orders was reflected in a mirror. Both oral and printed commands were executed slowly and imperfectly. He made several mistakes in writing down the nature of movements made by me, although he could imitate them without fail.

Condition in December, 1922, *seven years and ten months after he was wounded.*

He was in excellent general physical health. But the hallucinations which he described as "Nasty smell in mouth; make you sick like" had recurred about every fortnight. In April, 1921, they were followed by a definite epileptiform attack in which he became unconscious; further similar seizures occurred in August and November, 1921, and in October, 1922. The last of these was seen from start to finish by his parents. He was sitting on the sofa, when he lost consciousness and fell back struggling; he did not wet himself or bite his tongue, but the attack was accompanied by characteristic chewing movements. He complained that each seizure was preceded by the "nasty smell" and, when I inquired whether he had been troubled by vomiting, he replied, "Dirty, like be sick, makes me like sick and I can't; comes out of my mouth and nasty smell of it." Q.: "What comes out of your mouth?" A.: "Nasty smell. Try to be sick and can't. It might be two weeks, perhaps three weeks, might get 'em two, three days. The strength of my leg goes out of my leg when I'm like that."

TABLE IX.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Pictorial commands	Pictorial commands reflected in a mirror	Oral commands	Printed commands	Printed commands read aloud and executed		Writing down movements made by the observer
							He said :	Movement executed	
L. hand to L. eye	Correct	Perfect	Correct	Perfect	Slow, correct	L. hand to L. *ear*	Correct	L. hand to L. *ear*	Correct
R. hand to R. ear	,,	,,	,,	,,	,, ,,	Slow, correct	,,	Correct	,,
R. hand to L. eye	,,	,,	,,	,,	,, ,,	,, ,,	,,	,,	,,
L. hand to R. eye	,,	,,	,,	,,	,, ,,	,, ,,	,,	,,	L. hand to L. eye
L. hand to L. ear	,,	,,	,,	,,	,, ,,	,, ,,	,,	,,	Correct
R. hand to R. eye	,,	,,	,,	,,	,, ,,	,, ,,	R. hand to R. ear, eye	R. hand to R. *ear*	,,
L. hand to R. ear	,,	,,	,,	,,	,, ,,	,, ,,	Correct	Correct	L. hand to R. *eye*
R. hand to L. ear	,,	,,	,,	,,	,, ,,	,, ,,	,,	,,	Correct
L. hand to L. eye	,,	,,	,,	,,	L. hand to L. *ear*	L. hand to L. *ear*	,,	,,	,,
R. hand to R. ear	,,	,,	,,	,,	Slow, correct	Slow, correct	,,	,,	,,
R. hand to L. eye	,,	,,	,,	,,	,, ,,	,, ,,	R. hand to L. ear, eye	R. hand to L. ear; corrected	,,
L. hand to R. eye	,,	,,	,,	,,	L. hand to R. *ear*	R. hand, then correct	Correct	Correct	,,
L. hand to L. ear	,,	,,	,,	,,	Slow, correct	Slow, correct	,,	,,	L. hand to L. *eye*
R. hand to R. eye	,,	,,	,,	,,	,, ,,	,, ,,	,,	,,	R. hand to R. *ear*
L. hand to R. ear	,,	,,	,,	,,	,, ,,	,, ,,	,,	,,	L. hand to R. *eye*
R. hand to L. ear	,,	,,	,,	,,	,, ,,	,, ,,	,,	,,	Correct

He had suffered occasionally from pains in the head, and he pointed to the left half of the forehead and around the left eye. It was extremely difficult to discover their character, except that they made his head "thick"; he said, "Get out, lay down, go to sleep, sometimes goes away. If sit in kitchen, moving about working makes me getting worse on it."

Vision in the right eye was $\frac{6}{6}$, but there was no doubt that it was lost in the upper outer quadrant of the field. This scotoma had no definite boundaries, merging into parts where vision was defective. Disc and fundus were not abnormal.

Hearing was defective; a watch could be heard at a distance of 5 ft. on the right side, whilst in the left ear it was not even appreciated on contact. He said he heard a tuning fork, placed in the centre of the forehead, on the right side only; but over the left mastoid it was certainly audible, although the duration was shortened in comparison with the right.

Smell was grossly defective in both nostrils and he did not even react to ammonia.

Taste was good when the tongue was withdrawn into the mouth, but not when it was extended. This is not abnormal in an habitual smoker.

The pupil reacted well, there was no ocular paralysis, and face and tongue moved equally well on the two sides. The reflexes were normal, including the plantars and abdominals. There was no paresis, inco-ordination, tremor, change in tone, or any other motor affection. Sensation was perfect; appreciation of posture and passive movement, discrimination of two points, localization, recognition of differences in intensity, size, shape and weight, were equally perfect on the two sides.

Symbolic Formulation and Expression.

He was not in any way mentally defective; but a long course of idleness and inability to work had rendered him intellectually lazy. He lived on his pension in two rooms with his wife and child; she apparently talked to him very little and took no interest in his difficulties of speech. He never read a book or a newspaper.

Though he was still a willing witness and anxious to be examined, he was much more taciturn and less easily roused to say what he felt. He obviously recognized his disability in speaking and had grown used to remaining silent; but during our talks he became perceptibly brighter and more lively.

Articulated speech.—His speech was difficult to understand without the most careful attention. He was liable to begin with some odd sound and frequently passed on without attempting to pronounce the word correctly; he probably failed to recognize that it was incomprehensible to his auditor. I have given above several examples of this jargon, and his condition so closely resembled what it was during his first stay in the London Hospital that I formed the opinion he was degenerating in consequence of the epileptiform attacks.

He repeated certain sentences after me as follows: I have suffered from some headache lately became " I have suffered from headache " : On Saturday I had an attack, " On Sat-day I had attack " ; I find it difficult to speak, " I find it diff-cut to speak . . . I find to speak." I then asked him to say them over once again all together and he replied, " I had headache on Saturday . . . I can't zinc of thother " (the other). It was not so much the act of repetition which was at fault, but the power of retaining a phrase accurately in his memory sufficiently long to reproduce it.

Understanding of spoken words.—He certainly understood what was said to him and could carry out oral commands, although he was a little uncertain with the complex hand, eye and ear tests. But there was no doubt that he occasionally failed to follow something said by me in the course of general conversation in answer to one of his remarks, and his father still found it impossible to employ him for this reason.

Reading.—He chose a common object of colour and set the clock correctly to printed commands, but had more difficulty with the hand, eye and ear tests.

He could read aloud the simple phrases of the man, cat and dog test, but had profound difficulty with a consecutive paragraph (*vide infra*) ; his jargon became particularly evident, when he attempted to read aloud, and this led to great want of comprehension of the meaning of printed matter.

Writing.—He wrote his name and address together with that of his wife fairly well, although Emma was written " Emme " and Colchester Avenue shortened to " Colchester Ave."

The following letter written spontaneously to me was certainly worse than his previous efforts :—

" Dr. Head

just a line to you know I an allrigt as you ore the same. I for now Frank."

(This was evidently intended to be " Just a line to let you know that I am all right as I hope you are the same. I am for the present yours, Frank.")

He wrote badly to dictation but copied a long paragraph without a single mistake.

Printed paragraph read silently or aloud, written and narrated.—I somewhat modified the procedure adopted in 1920, in order to make this test more specific. I gave him the following printed legend without its accompanying picture. " During the War a box was placed on the platform at Snaresbrook Station as a receptacle for flowers for the wounded. Many of the passengers brought nosegays daily from their gardens and these were sent to the Bethnal Green Infirmary." This he read silently and could tell me only, " During the War . . . there was some flo-wens at Station . . . Horspedl, I think . . . some green . . . No, can't zinc no more."

He read it through again to himself and wrote, " Do the war ther was fowers for the hoseple at the at the Gren."

He took the paper into his hand again and read aloud : " Durin the war . . . a box . . . was placed on . . . on the plaf-orm . . . at . . . can't memb' it . . . station . . . as a . . . no sir, can't get it . . . for flowers . . . for the . . . woun-ed . . . many of the . . . passengers . . . brought . . . no-gays . . . daily . . . from the gardens . . . and those were sent . . . to the . . . Bet-nel Green . . . In-fir-mary."

I then said, "Tell we what you have understood?" He replied, "Some flowers for the wounded . . . in the Hospedl . . . the Hospital . . . No, sir."

To my dictation he wrote, "Doing the war a box was Place on the plapfon at slaion as a resel for flers for the wooded. Many of the stition brout nosgays daily from thir garnen lhes (these) wer sent to the Belnol Gren Infemer."

But, when asked to copy this paragraph in cursive handwriting, he carried out the task perfectly without a single mistake.

Asked, however, what he had understood he could only reply, "Got to the stashn . . . for some flowers . . . for the wounded Horpedls . . . at Burnel Green . . . ain't it . . . Bur-nal Green."

Numbers and arithmetic.—He counted slowly and deliberately up to 30, and I noticed no defects of pronunciation until he came to "thirty-tree" (thirty-three). He continued correctly up to 39, but, instead of saying "forty," began the thirties over again, reaching 44 without a mistake. From this point he became uncertain, saying, for instance, "62, 64, 66, 57, 58, 59, 60"; he was perpetually thrown out of his stride and tempted thereby into some false sequence. At 70 he broke down altogether, saying "No, I can't think more."

Addition.

215	..	238	..	385	
324	..	424	..	638	
429		6312		91113	

Subtraction.

234	..	281	..	512	
123	..	168	..	389	
111	..	124	..	3	Then gave up.

Coins and their relative value.—All the coins were named correctly and their relative value was given without fail, though rather slowly. When shopping he had no difficulty with change, as far as I could gather from his relatives.

Drawing.—He drew a good picture of a spirit-lamp both from the model and subsequently from memory. Asked if he could "see the lamp," when drawing from memory he replied, "See whole lamp and glass . . . and glass . . . bit of string to light it" (the wick). But he drew an extremely poor representation of an elephant without trunk or tusks.

His ground-plan of the room in which we worked was on the other hand accurate in every particular.

Serial Tests.

It is interesting to notice how exactly these observations bore out the results obtained more than two years earlier, a testimony to the trustworthiness of the methods employed.

(1) *Naming and Recognition of Common Objects* :—

TABLE X.

	Pointing to object shown	Naming	Oral commands	Printed commands	Writing name of object indicated
Knife	Perfect	Correct	Correct	Correct	kinfe
Key	,,	,,	,,	,,	key
Penny	,,	,,	,,	,,	Pomey
Matches ..	,,	,,	,,	,,	Mahey
Scissors.. ..	,,	,,	,,	,,	Cyses
Pencil	,,	,,	,,	,,	ponsel
Key	,,	,,	,,	,,	key
Scissors.. ..	,,	,,	,,	,,	Cyses
Matches ..	,,	,,	,,	,,	Mayes
Knife	,,	,,	,,	,,	knefe
Penny	,,	,,	,,	,,	poney
Matches ..	,,	,,	,,	,,	Moyes
Scissors.. ..	,,	,,	,,	,,	Cyses
Pencil	,,	,,	,,	,,	ponsel
Penny	,,	,,	,,	,,	Poney
Knife	,,	,,	,,	,,	knefe
Key	,,	,,	,,	,,	key
Pencil	,,	,,	,,	,,	ponsel

All these tests were carried out perfectly except when he attempted to write the name of an object indicated; then his spelling became worse than might have been expected from the state of his education and the words were curiously malformed.

(2) *Naming and recognition of colours* :—

TABLE XI.

	Pointing to colour shown	Naming	Oral commands	Printed commands	Writing name of colour indicated
Black	Perfect	Correct	Correct	Correct	Block
Red	,,	,,	,,	,,	Red
Blue	,,	Bĕ-lew	,,	,,	Bue
Green	,,	Correct	,,	,,	Gran
Orange	,,	,,	,,	,,	Oren
White	,,	Whide	,,	,,	whit
Violet	,,	Brown	,,	,,	Velen
Yellow	,,	Yeller	,,	,	Yolow
Red	,,	Correct	,,	,,	Red
White	,,	,,	,,	,,	whit
Yellow	,,	,,	,,	,,	Yolow
Blue	,,	,,	,,	,,	bue
Green	,,	,,	,,	,,	Grem
Black	,,	,,	,,	,,	Blok
Orange	,,	,,	,,	,,	Oren
Violet	,,	Brown	,,	,,	Valen

His choice to oral and printed commands was excellent, but his pronunciation of the names was not perfect and, on attempting to write them down, the words were badly formed. Throughout, the more abstract colours gave him greater difficulty than the concrete names of common objects.

(3) *The man, cat and dog tests* :—

TABLE XII.

	Reading aloud	Repetition	Reading from pictures	Writing from pictures	Writing from dictation	Copied from print in cursive script	Reading aloud and writing	
							He read	He wrote
The dog and the cat ..	Correct	Correct	Cat . . . dog	Cat and dog	The dog and cat	Perfect	Correctly	The cat and dog
The man and the dog ..	,,	Man and dog	The dog and the man	man and dog	The man and dog	,,	,,	The man and the dog
The cat and the man ..	,,	Cat and the man	Cat and the man	Man and Cat	The man and cat	,,	,,	the cat and man
The cat and the dog ..	,,	Cat and the dog	Dog and the cat	Cat and dog	The cat and dog	,,	,,	the cat and dog
The dog and the man ..	,,	Correct	Dog and the man	Dog and man	The dog and man	,,	,,	the dog and cat
The man and the cat ..	,,	,,	Cat and the man	Man and cat	The cat and man	,,	,,	the man and cat
The dog and the man ..	,,	Dog and the man	Man and the dog	Man and dog	The dog and man	,,	,,	the man and dog
The cat and the man ..	,,	Correct	Man and the cat	Man and cat	The cat and man	,,	,,	the cat and man
The dog and the cat ..	,,	,,	Dog and the cat	Dog and cat	The dog and man	,,	,,	The cat and dog
The man and the dog ..	,,	Man and the dog	Man and the dog	Man and dog	The man and dog	,,	,,	the Man and dog
The cat and the dog ..	,,	Cat and the dog	Cat and the dog	Cat and dog	The cat and man	,,	,,	The cat and dog
The man and the cat ..	,,	The man and a cat	Man and the Cat	Man and cat	The man and cat	,,	,,	The man and dog

He read aloud and copied these simple phrases perfectly and made no definite mistakes in repeating the words after me. But, with every other form of this test, he showed the same extraordinary tendency to alter the sequence of the two nouns, which was so apparent in previous observations. On reading from pictures he frequently went from right to left instead of in the usual direction, and this reversal occurred, even when he wrote the words to my dictation. Similar mistakes in writing occurred after he had read each phrase aloud : for, although he said exactly what was put before him in print, he made many errors in the sequence of the words he wrote.

(4) *The clock tests* :—

TABLE XIII.

	Direct imitation	Telling the time	Oral commands	Printed commands (both ordinary nomenclature and railway time)	Writing down the time shown on a clock
5 minutes to 2 ..	Correct	Five to two ..	Correct	Correct	Five to to
Half past 1 ..	,,	Half past one ..	,,	,,	half pas one
5 minutes past 8 ..	,,	Fi pās eight ..	,,	,,	Five pas Eigt
20 minutes to 4 ..	,,	Twenty to four ..	,,	,,	temy to fur
10 minutes past 7	,,	Ten past seven ..	,,	,,	Ten pas sevn
20 minutes to 6 ..	,,	Twenty to six ..	,,	,,	temy to sex
10 minutes to 1 ..	,,	Ten to one ..	,,	,,	Ten to One
A quarter to 9 ..	,,	Qūār to nine ..	,,	,,	45 to nie
20 minutes past 11	,,	Twenty pās leven	,,	,,	Temy past 11
25 minutes to 3 ..	,,	Twenty five to three	,,	,,	35 to tre

He set a clock to oral and printed commands and told the time correctly : his only faults were those of pronunciation. When he attempted to write down the time, his spelling was remarkably bad and he tended to adopt an abnormal nomenclature, such as " 45 to 9 " instead of " a quarter to nine."

(5) *The hand, eye and ear test.* (See Table XIV.) :—

He imitated my movements slowly, when we sat face to face, and made a few mistakes in executing pictorial commands ; but he was extremely quick and accurate if either form of order was reflected in a mirror. He wrote down imperfectly movements made by me, sometimes reversing the order of hand and eye or ear. Oral and printed commands were also carried out somewhat slowly and in these tests he made several errors.

§ 4.—*A Case of Nominal Aphasia due to Gunshot Injury of the left Angular Gyrus. Nearly five years later, in spite of profound recovery o o speak, to read and to write, the character of the defects in symbolic formulation and expression was essentially unchanged.*

No. 7.—Gunner Aloysius McN., aged 22, was wounded in the head by a fragment of a high-explosive shell, on October 15, 1917. He was admitted on the same day to the 3th Australian Casualty Clearing Station, where an operation was performed and the following notes made. " Shell wound of the left parietal

TABLE XIV.

	itation of movements made by the observer	Imitation of movements reflected in a mirror	Pictorial commands	Pictorial commands reflected in a mirror	Oral commands	Printed commands	Writing down movements made by the observer	Copying printed commands in cursive script
L. hand to L. eye	correct	Perfect	Correct	Perfect	Correct	Correct	Left eye hand left	Perfect
R. hand to R. ear	,,	,,	,,	,,	,,	,,	Rigt ere Rigt	,,
R. hand to L. eye	Very slow, corrected	,,	Reversed	,,	,,	,,	Rigt eyr Rigt	,,
L. hand to R. eye	Slow. correct	,,	Corrected	,,	,,	,,	left Rigt Eye	,,
L. hand to L. ear	,, ,,	,,	Slow, correct	,,	,,	,,	left Ere left hand	,,
R. hand to R. eye	,, ,,	,,	,, ,,	,,	R. hand to R. *ear*	,,	Rigt Eye Rigt hand	,,
L. hand to R. ear	,, ,,	,,	,, ,,	,,	Correct	L. hand to L. ear	left hand left Ere	,,
R. hand to L. ear	,, ,,	,,	,, ,,	,,	,,	Correct	Rigt hand left Ere	,,
L. hand to L. eye	,, ,,	,,	R. hand to L. eye	,,	,,	,,	left hand left Eye	,,
R. hand to R. ear	,, ,,	,,	Correct	,,	,,	,,	Rigt hand Right Ere	,,
R. hand to L. eye	,, ,,	,,	,,	,,	,,	R. hand to L. *ear*	Rigt hand left Eye	,,
L. hand to R. eye	,, ,,	,,	,,	,,	,,	Correct	left hand left Ege	,,
L. hand to L. ear	,, ,,	,,	,,	,,	L. hand to R. ear	,,	left hand left Ere	,,
R. hand to R. eye	,, ,,	,,	Reversed	,,	R. hand to R. *ear*	,,	Right hand Rigt Eye	,,
L. hand to R. ear	,, ,,	,,	Correct	,,	Correct	L. hand to R. *eye*	Rigt hand Rigt Ere	,,
R. hand to L. ear	,, ,,	,,	,,	,,	,,	Correct	Rigt Ere Rigt hand	,,

bone. Large compound depressed fracture. Laceration of the dura. Protrusion of brain substance. Loose bits of bone were removed including the margins of the fracture, but no foreign body."

On October 18 he was admitted to No. 12 General Hospital, where he remained until November 23. The field card bore the following record of this period:—

"October 29. Wound in the parietal region discharging pus profusely. Speech impaired.

"October 30. Disc edges are both less sharply outlined than at the previous examination, but no definite choking can be made out. Patient is more stuporous this morning and headache more pronounced and more sharply localized.

"November 1. Small operation to increase drainage. Anterior margin of the wound incised. Free discharge of pus began this morning. Almost complete recovery of use in the right arm. Speech also returned.

"November 3. Wound draining well. Speech improving. Talks a good deal: still unable to say certain words. Movements of the right arm good, but there is still some weakness.

"November 9. Draining freely through three rubber tubes. Speech gradually improving.

"November 21. Discharge considerably abated. Speech fairly good. No complications."

Throughout his stay in this hospital the temperature did not rise above normal limits.

He was admitted to the London Hospital under my care on November 24, 1917, with a superficial granulating stellate wound in the left parietal region, which pulsated heavily. The anterior limit was level with a point 19·5 c.m., along the nasion-inion line; posteriorly the wound extended further backwards for 7·5 cm. In front it was 7 cm., behind 9 cm., from the middle of the scalp. The total nasion-inion measurement was 34 cm., and this was transected by the interaural line at a point 14 cm. from the root of the nose. (Cf. figs. 4 and 5, pp. 406 and 407.)

An X-ray photograph showed an area of removal of bone in the anterior parietal region measuring 4 cm. by 2 cm. at its broadest part, with a fissured fracture running directly forwards.

Pure cultures of staphylococcus only were obtained from the wound. It was firmly healed by December 10, 1917.

On admission he was so grossly aphasic that it was impossible to obtain from him any information with regard to his injury or subsequent events. The words he uttered were comprehensible, but he could not find the means to express himself in speech or writing. Throughout, the character of his disabilities remained the same, although he rapidly regained sufficient facility in utterance to make more extensive observations possible.

He had not been the victim of convulsions or seizures of any kind, and although he still suffered from considerable headache, he had not vomited since October 20.

His vision was $\frac{6}{6}$ and the optic discs and fundi were in every way normal. Hearing, smell and taste were unaffected.

The pupils reacted well. There was no ocular paralysis or nystagmus. Movements of the face and tongue were normal.

All the deep reflexes were equal on the two sides, the abdominals were brisk and the plantars gave a downward response.

There was no paralysis or paresis; tone was not affected and the movements of the limbs were neither inco-ordinate nor ataxic.

At this stage it was impossible to test sensation or to map out the visual fields; but subsequent examination showed that they were normal and that sensibility, even to measured tests for recognition of passive movement, discrimination of the compass-points, localization of the spot touched, and appreciation of differences in form, was not affected.

Condition between December 10, 1917, *and February* 11, 1918, *eight to seventeen weeks after he was wounded.*

He was a well-built healthy young Scotchman, who had lived all his life in Yorkshire. He had been originally employed in the steel works, but, finding he possessed a powerful baritone voice, he had taken to the music hall stage, where he sang sentimental songs. When first admitted, he was puzzled and frightened by his lack of power to express his thoughts. But he soon settled down and became a contented and popular patient, most helpful in the daily life of the ward.

Symbolic Formulation and Expression.

Articulated speech.—He had little power of spontaneous speech; but if a question was put to him, he answered intelligently, so far as the paucity of words at his disposal permitted. For instance, asked his age, he replied, "Twenty . . . twenty . . . two."

Q. "What did you do before enlisting?"

A. "I was in . . . Middle . . . Middle . . . boro . . . stale . . . steel . . . yes, steel . . . walk . . . work . . . I can't bring it out." I suggested "steel-works?" and he said "Yes, yes . . . that's it."

Q. "You used to sing, didn't you?"

A. "Yes . . . yes . . . when I was young . . . about ni . . . about twelve . . . when I was about twelve . . . but then I went to the steel . . . I can't get it."

Q. "Can you remember any of the songs you used to sing?"

A. "I've always tried . . . to see if I could think of them . . . but I've never been able to think of any of them. I used to think of them . . . . before I went over" (waving his hand to show that he meant over the top) ". . . I used to say them . . . but now . . . since" (putting his hand to his wound) ". . . since that . . . I can't even think."

Throughout this last answer intonation and expression were almost normal and his gestures showed that he had been vividly excited by my question. When in doubt he moved his lips silently, as if seeking for a word in which to express himself. If he could find the phrase he required, the syntax was perfect and the syllables were touched off correctly.

Asked his name he said "MacNally" correctly, but could not precede it by the somewhat difficult "Aloysius"; for his address he simply repeated several times in succession "Middle, Middle-boro" (Middlesbrough).

He was entirely unable to say the months or days of the week spontaneously in order.

He could not repeat the names of common objects or colours exactly, although the sounds he uttered usually bore a distinct relation to the words said by me. Thus for scissors he said "Sis" or "Sit, sitty, sizz": knife became "Nike" or "Night, nie, a nie"; black was "Blat, berlat, blad" and orange "Od-je, od-inge, orridge." In the same way attempts to repeat the months after me produced the following results:—

January: "Jan-jer-ley, Jan, Jan."
February: "Fenchurch, Jan-jey, Jan-jey."
March: "Mart, Mar, Mar, Marts."
April: "What was it? Aper, Aperl."
May: "Mage, Made, Mage."
June: "Ju, June."
July: "June, June, Jun-eye."
August: "Orgeons, Or-just."
September: "Eps-ten, Ex-pent, Ex-penst."
October: "Ex, Ox, Ox, Ox-toe, Ox-tove."
November: "No-vendl, New-vender."
December: "Ex. What was it? Ex-pend. Ex-cembr."

When he attempted to repeat the simple phrases of the man, cat and dog tests he succeeded after much hesitation; once, however, he made the characteristic mistake of responding with a wrong combination, substituting "the cat and the man" for the dog and the cat.

Comprehension of spoken words.—He showed obvious defects in comprehending spoken words and phrases; choice of a common object or colour was slow and he frequently gave up the attempt altogether. He set the clock and carried out the coin-bowl test badly to oral commands. He made many mistakes in executing the complex choice between hand, eye and ear, although simpler commands of a similar kind were carried out, with one exception, correctly.

Reading.—He had considerable difficulty in comprehending the significance of single words put before him in print, selecting common objects or colours slowly and with obvious effort; often he gave up all attempt to make a choice. He set the clock badly to printed commands and confused "past" and "to" the hour. In the same way he frequently failed after several attempts to place the proper coin into the right bowl. Simple orders, such as "Shut your eyes," "Put our your tongue," presented to him in print, were poorly executed and he failed grossly to perform the more complex choice demanded by the hand, eye and ear tests.

He read aloud the names of the colours with difficulty and his pronunciation was extremely defective. But the words, badly formed as they were, evidently conveyed their proper significance; for the choice he made was more accurate than when he was not permitted to utter them aloud.

Even such simple words as the man and the dog were defective, when evoked to response to pictures. The man became "mand, mant," the dog was called "got, god, gone," whereas the cat was always pronounced perfectly. When he attempted to read these simple phrases from print, the results were even worse and he struggled ineffectively to find the correct expressions.

Asked to read the orders of the coin-bowl test aloud, he converted them into simple numbers; for example "the second into the third" became "two into three"; but this did not materially improve the way in which he executed the task set him in print.

Simple commands, such as "touch your nose," &c., were read aloud extremely badly and the movements made in response were no better than if he executed them in silence.

Writing.—With great effort he succeeded in writing spontaneously "McNally A." and "A McNally, mid," but could get no further in his address. Wishing to write to his mother he began "Mothr, I" and then ceased altogether.

To dictation he wrote "Aloi——McNally, 22. Ba——Steer, Middes"; he was unable to finish either his Christian name or any part of his address. But, in response to a printed copy, he produced the following, in cursive handwriting, with interjected capitals:—

"Aloysius McNally,
28 Balekow street [t's uncrossed]
MiddleBoRough."

He was unable to write down the name of any one of the colours shown to him, although he copied them from print without a mistake. Here again he employed cursive script, interspersed with irrelevant capitals.

The words, corresponding to any two pictures of the man, cat and dog test, were written correctly and in most instances he inserted the definite articles. He copied these phrases from print in perfect handwriting, slowly and without error of any kind.

Although he employed numbers only, he expressed the time extremely badly in writing. Frequently he wrote the hour, but failed altogether to indicate the minutes shown on the clock-face.

Writing to dictation was almost impossible, as can be seen from his attempts to write his name and address. When the simple phrases of the man, cat and dog test were dictated to him, his written response was in every instance incomplete.

The alphabet.—Asked to say the alphabet, he began very slowly "A B C";

then after a pause he continued "E F F Jay (evidently intended for G) H F did I say F? I forget the next one." He made several more attempts without further success.

He could repeat the alphabet after me slowly, but I was compelled to say each letter several times. On the first occasion his lips would move, although he uttered no sound, not even a whisper: when I again said the same letter, he pronounced it accurately, though with some effort.

Separate letters were read aloud correctly, bearing in mind his Scotch accent.

He could copy the alphabet in capitals; but, when he attempted to write it spontaneously, he was only able to produce with great effort the following sequence: "A E C D f J."

To dictation he wrote extremely slowly and, in almost every instance, it was necessary to say the letter more than once. During this test his lips moved although he uttered no sound.

Numbers.—Asked to count, he started quickly and correctly, but rapidly slowed down and ended in confusion, "five, six, seven, nine, seven, eight, nine, nine, ten, ten, twelve, fourteen." He then began again with the following result: "one, two, three, four, four, five, six, seven, ny, nine, ten, eleven, ten, twelve, four, four, twelve, four-teen, seven, seven, seven-teen." I suggested he should begin at twenty and he said "Twenty, one, two, three, four, five, seven, eight, eight, ten"; throughout he never repeated the word twenty, but counted the decade as if he was starting from one. I asked "What is twenty and ten?" and he replied "Twenty ten, twenty ten, thirty." He then started to count at thirty, saying "Thirty, twenty-one, thirty, thirty-two, twenty-two, twenty-thirty, twenty, no, thirty-two, twenty-three, thirty-four, twenty-six, twenty-five, twenty-seven, thirty, thirty, thirty-eight, thirty-seven, thirty-six, no, thirty-nine."

Arithmetic.

Addition.

123	228	..	..	..	345	
214	734	..	..	..	868	
337	9512	He said "twelve," "five," "nine," and wrote them down independently.			11 10 12	Again he said "twelve," "ten," "eleven," writing them down independently.

Subtraction.

685	..	..	752	..	..	821
342	..	..	536	..	..	467
342			224			446

Throughout he subtracted the lower from the higher number, oblivious of whether it was in the top or bottom line.

Coins and their relative value.—A series of coins were laid upon the table and he named them as follows:—

Penny	"Pen-ny."
Sixpence	"Six . . . six . . . six-pence."
Two-shilling piece	"Shill-un . . . no, two . . . two shill-un."
Shilling	"Shill-un."
Threepenny piece	"Six . . . no, three . . . shill-un . . . three penny."
Shilling	"Shell . . . shill-un, shill-un."
Sixpence	"Six . . . six-pence."
Two-shilling piece	"Shill-un . . . two . . . two shillun."
Threepenny piece	"Six . . . three six . . . thrup . . . threp . . threp-pence."
Penny	"Pen-nuth . . . penny . . . pen . . . penny."

Two coins were then placed before him and he was asked how many of the one went to make the value of the other. He answered as follows:—

One penny and sixpence	"Six."
One penny and threepence	"Four . . . penny . . . four . . . fourpence." (He evidently added the two coins.)
A sixpence and a shilling	"Six . . . sixpence . . . shillun . . . six . . . sixpence.
A shilling and a two-shilling piece	"Three shillun" (I then asked the question again and he replied "Shillun").
A penny and a sixpence	"Six . . . six."
A penny and a shilling	"Shillun . . . six . . . sixpence" (question repeated) "Six."
A penny and a threepenny piece	"Three . . . three pennies."
A threepenny piece and a sixpence	"Sixpence" (question repeated) "Six . . . two . . . two . . . sixpence."
A sixpence and a two-shilling piece	"Two . . . two . . . two shillun" (question repeated) "Four . . . no . . . four six . . sixpence."

But, in spite of these confused replies, he undoubtedly rocognized the monetary value of each of these coins, provided he was not compelled to express their relation to one another in words. For he was able to put together the equivalent of any one of them from amongst a heap of money on the table in front of him. Thus, when given a shilling, he picked out a sixpence, added a threepenny piece and then piled three coppers (pennies) one on the other, making in all a shilling; with a two-shilling piece, he chose a sixpence, a threepenny bit, a shilling and then slowly added three coppers to complete the correct sum.

Drawing.—He made a poor outline drawing of a spirit-lamp placed before him and did not attempt to represent the mechanism of the burner and wick. This, with all its faults, he reproduced from memory after removal of the model.

But, when I drew a picture of the same object, he made a faithful copy not only with my drawing in front of him, but also from memory, although he tended to detach the lower part of the wick from the burner.

Asked to draw an elephant, he produced an absurd figure. I asked if he would like "to put in anything" he had omitted; he replied "Yes, doctor, but

I don't know where to put it." To the question "What is it?" he placed his forefinger on the head, but said nothing.

I then drew the outline of an elephant without trunk, tusks, eye or ear. Giving him the pencil, I asked him if there was anything he would like to add; he marked in crudely the parts I had omitted. Told to name them, he said "Near" (ear), "Eye" and for trunk "I know what it is, but I forget what they call it." Q. "What does he do with it?" A. "His mouth" (placing his right hand to his own mouth). When I pointed to his drawing of a tusk, he replied "I know what it is, but I can't say what it's called . . . trunt trunce . . . I forget that." Q. "What does he do with it?" A. "Eat it . . . your mouth," touching his teeth with his hand.

Orientation and plan-drawing.—He found his way about the hospital with ease and, when taken into a room apart, evidently had an accurate conception of the relation of his bed to the other objects in the ward. But he failed to draw a satisfactory ground-plan, although he made marks on the paper indicating the true position of the cupboard, windows, door and the neighbouring unoccupied bed.

In the middle of a sheet of paper I drew a rectangle, to represent his bed, with a human figure lying upon it. He was able to point out accurately the relative situation of the surrounding objects, adding the following explanatory remarks. "There's a bed, no one there now"; on the other side "No other bed, there's only my bed"; he pointed below the foot saying "The war (wall), the rawd, the door, yes the door." Asked what was above the head of the bed, he struck with his hand the wall of the room in which he was being examined, saying "The, the, war." He indicated the cupboard in its correct position, exclaiming "I never can say that . . . form close . . . clothes."

Games.—With dominoes he was slow in fitting the numbers together in series, although he made no actual mistakes. His conception of the task was perfect, but he kept looking backwards and forwards from the last domino to the heap on the table, evidently unable to keep in his head the number he required. When he picked out the right one from the pool, he brought it close to the piece already in place in order to be certain that it bore the number he required. He worked on silently and steadily with no uncertainty of aim.

He played a game of draughts correctly, making the moves necessary to avoid the loss of his pieces; he had little power of playing for position. He cleverly avoided the traps I set him and never missed taking one of my pieces that fell his way, although he did not see how to force me to give him two for one.

Singing.—Before he joined the army he was on the music hall stage as a singer of serious and sentimental songs. He had never been able to read music quickly from notes and was accustomed to learn mainly by ear. At the time he was under my care, he seemed to be completely unable to read musical notation. But, if he was given the opening notes of a song he had known, he sang it through accurately without words. Time, tune and modulation were perfect and his voice had the full volume of a powerful high baritone. He could not, however, sing any song, if he attempted to pronounce the words.

Serial Tests.

(1) *Naming and recognition of common objects* :—

TABLE I.

	Pointing to object shown	Oral commands	Printed commands	Naming an object indicated	Duplicate placed in hand out of sight	Repetition	Copying from print
Key ..	Correct	Correct	No response	Impossible	Correct	K . . . chay	In capitals only
Knife ..	,,	"I missed that. Say it again." Correct on repetition	Correct	,,	,,	Nike . . . nike	,,
Match Box	,,	Correct	Correct; great hesitation	,,	,,	Mat . . . mats . . . mert	,,
Penny	,,	"I don't think I heard that"	"Can-na"; gave up	,,	,,	Pen . . . penny . . . palty	,,
Scissors	,,	Correct	Gave up	,,	,,	Sis	,,
Pencil	,,	,,	Correct	,,	,,	Pen . . . pent	,,
Key ..	,,	Gave up	"Can't"; gave up	,,	,,	Kay	,,
Knife ..	,,	Correct	Correct	,,	,,	Night . . . nie . . . a nie	,,
Match Box	,,	,,	Correct; very slow	,,	,,	Matze . . . mat . . . mack . . . mat	,,
Penny	,,	,,	Gave up	,,	,,	Pen . . . penny	,,
Scissors	,,	No reply	"Don't think I know it"	,,	,,	Sit . . . sitty . . . sizz	,,
Pencil	,,	Correct	Correct, but uncertain	,,	,,	Pen . . . pentil . . . pint-ua	,,

He was completely unable to name a single object presented to him; he did not even make imperfect attempts to do so, but ejaculated some such expression as "It's a . . . I know if I could say it," "I think I would know it, but I couldn't . . ." "I ken, but I can't say it."

He had great difficulty in repeating the names said by me, although his utterances usually bore some imperfect relation to the correct word.

He chose the right object quickly, when a duplicate was shown to him or placed in his hand out of sight.

But selection to oral or printed commands was very imperfect.

When I placed any one of these common objects into his hand and asked "What is it for?" he used it correctly with singularly appropriate gestures.

(2) *Naming and recognition of colours.* (See Table II.) :—

He could not give names to the colours and fell into such errors as calling black blue, or orange red. But his greatest difficulty was to find the appropriate words and in several instances he gave up the attempt. Repetition was extremely defective.

TABLE II.

	Pointing to colour shown	Oral commands	Printed commands	Naming	Repeating the names of the colours	Writing name of colour indicated	Copying names from print	Printed names read aloud and colour chosen	
								He said :	He chose :
Black . .	Correct	Correct	Correct	Blue . . no, blay . . lack . . ack . . luff	Bŭ-lack	ba	Black	Be-lack	Correctly
Red . .	,,	Doubtful, finally correct	,,	I don't know whether I could say it	Lead . . ret . . red	Ke	Red	Led . . red	,,
Yellow	,,	"I don't know"	"I don't know"	I could only think of what it was	Leller . . lead-o . . li-go	gn	YeLLow	Bell-a	,,
Blue . .	,,	Correct	No choice	Loo . . loo . . loo	Ber-loo	B	BluE	Berew . . brew	"I don't know which one it is"
White	,,	,,	Doubtful, finally correct	Why . . white	Why . . white	hwi	WHiTE	Why	Correct
Orange	,,	Yellow	Yellow	Ride . . rite	Oag-inge . . ollidge	—	Orange	Orrig	,,
Violet	,,	"I don't think I know"	"I don't know"	I forget that	Valley. . val-edge . . vi-et-chek	wi	Violet	Wy . . wall wall-et	,,
Green	,,	No choice	Blue	I don't get them right	Glee . . glee . . green	ge	green	Reed	,,
Black . .	,,	Correct	Correct	Lad . . blad	Blat . . berlat . . blat	Ba	Black	Brack	,,
Red . .	,,	,,	Orange	Rite . . I can't say what I think	Gred . . ger-ed	w	Red	Ru . . red	,,
Yellow	,,	Doubtful, finally correct	Correct	Ref . . rite	Gerons . . ger-letchy . . kellow	ge	Yellow	Ledder . . redder	,,
Blue . .	,,	No choice	Green	Blute . . blue	Ber-loo	gule	Blue	Loo	,,
White	,,	Correct	Very slow, correct	Will . . wit . . will . . light	Whide	wh	white	Wy . . wide	,,
Orange	,,	Doubtful, finally correct	"I forget which one"	Red	Od-je . . cd-inge . . orridge	r	ORange	Rod-ji	,,
Violet . .	,,	Correct	Blue	Was it blowit . . blute?	White	bu	Violet	Wy-el-et	,,
Green . .	,,	Doubtful, finally correct	Correct	I think I know it	Ger-ee . . keree . . gree	gee	green	Ree	,,

TABLE III.

	Reading aloud	Writing from dictation	Writing from pictures	Reading from pictures	Repetition	Copying
The cat and the man	Dē . . carnt . . art . . that . . mart	tat the Man	the Cat the Man	A cat . . the mand, man, mant	Correct	Correct
The dog and the cat	Dē . . god . . and the . . cat	the dog the cat	dog cat	Got . . a god . . cat	The cat . . the cad and the man	,,
The man and the dog	The . . măt . . and . . these, the . . gone, gone, got	the ca	the man the dog	Mand . . got, the gone, dog, dog	Correct	,,
The cat and the dog	Dē . . găt, gone, cat . . and . . ee . . dot	the cat and the god	the cat the dog	Cat . . god, dog	,,	,,
The man and the cat	Thēte . . mat, mant, mand . . and . . then . . cad, cat	the man and the cat	the man the cat	Man . . cat	The man . . the man and the . . cat (correct)	,,
The dog and the man	The . . gond . . and . . the . . mem, man	the god and the man	the dog the man	Dog . . mant, mand, a man	The dog . . the dog . . the dog and the . . and the man (correct)	,,

Choice to oral and printed commands was also imperfect: but he responded better if he was allowed to read the names aloud.

He could not write any one of them completely in response to a colour shown to him. All the names were, however, copied correctly from print in cursive handwriting, broken by irrevelant capital letters.

(3) *The man, cat and dog tests.* (See Table III.) :—

He read aloud these simple phrases in an extremely imperfect manner; the sounds showed that he was striving to render the correct content, but the words were scarcely recognizable. Reading from pictures was executed somewhat better and, when he repeated the words said by me, he made one serious mistake only. This was however characteristic, for he substituted "the cat and the man" for the dog and the cat.

He wrote almost equally badly from dictation and from pictures; but every phrase was perfectly transcribed from print into cursive handwriting.

(4) *The clock tests*:—

TABLE IV.

	Direct imitation	Oral commands	Printed commands	Telling the time	Writing down the time
A quarter to 9 ..	Correct	Correct	Correct	"I could get it, if I could say it"	9
10 minutes to 1 ..	,,	,,	Both hands at 1	"I can't say it"	12.10
20 minutes past 11	,,	Both hands at 11	Correct	No reply	11
Half past 1 ..	,,	Both hands at 1	,,	"Yes, one"	1.30 (correct)
5 minutes to 2 ..	,,	Both hands at 2	,,	"Two, two"	1 "I've lost that one"
10 minutes past 8	,,	Short hand at 8; long hand at 12	,,	"Aye, ayte"	8.10 (correct)
20 minutes to 6 ..	,,	Both hands at 6	Set 6.20	"Fye, isn't it?"	5
Half past 2 ..	,,	Correct	Set 2.15. "I don't think I got that one"	"Two, six; is that six?" pointing to long hand	2.30 (correct)
20 minutes past 9	,,	,,	Correct	"Nine is it? and four was it?"	9 "I don't know what that is," pointing to long hand
10 minutes past 7	,,	Short hand at 7; long hand at 12	,,	"Seven . . two," pointing to long hand	7.10 (correct)
20 minutes to 4 ..	,,	Short hand at 4; long hand at 10	Set 4.20	"Four . . ayte," pointing to long hand	3
10 minutes to 7 ..	,,	Correct	Set 7.10	"Seven . . ten"	6.10
A quarter past 9 ..	,,	Short hand at 9: long hand at 12	Short hand at 9; then completely puzzled	"Nine . . three"	9.15 (correct)
20 minutes to 3 ..	,,	Correct	Short hand at 3; then puzzled	"Two . . ayte"	2 "I can't get that"
5 minutes past 8 ..	,,	,,	Correct	"Ayte . . one"	8.5 (correct)

He set the hands of one clock in direct imitation of those of another without a mistake of any kind. His lips did not move, but he looked backwards and forwards frequently from the model to the clock he held in his hand.

Both to oral and printed commands he made many errors, obviously misunderstanding the order given and occasionally setting both hands at the same point.

There were many gross defects, when he attempted to tell the time aloud, and he frequently failed altogether. Occasionally, instead of the number of minutes indicated by the long hand, he would give the hour at which it stood; for instance, 9.15 was called "nine three," 8.5 "eight one." He also wrote the time shown on the clock extremely badly.

Here it was not the power of forming words that was at fault, but comprehension of their full significance for internal use and when they were presented to him orally or in print.

(5) *The coin bowl test:—*

TABLE V.

	Oral commands	Printed commands (not read aloud)	Printed commands read aloud	
			He said:	Movement executed
2nd into 3rd	Correct, slow	Correct	Two, three	Correct
1st into 3rd	,, ,,	Correct; slow	Won, tree	,,
2nd into 1st	2nd coin . . "I forget which one" (repeated) correct	1st coin . . 2nd coin . . No further action	Two, won	1st into 1st
3rd into 2nd	3rd coin . . "I forget" (repeated) correct	2nd into 3rd	Ree, tree, two	3rd into 3rd
1st into 4th	1st coin; (repeated) correct	Correct; slow	Won, four, four	1st coin . . "Was it four?"; did nothing
4th into 3rd	3rd into 2nd	3rd into 4th	Four . . one, ree, tree	3rd into 3rd
2nd into 4th	Correct	Correct	Two, four	Correct
4th into 1st	4th coin . . "I forget" (repeated) correct	,,	Four, won, won	1st into 4th
3rd into 1st	Correct	3rd coin . . "I forget which one I've got"	Tree, won, tree	Correct
1st into 2nd	2nd into 1st	Correct	One, two, two	,,
3rd into 4th	Correct, slow	3rd coin . . "I forget which one to put it in"	Three, four	3rd into 3rd
4th into 2nd	"I forget which it was" (repeated), 4th into 1st	Correct	Four, taw	Correct

Oral and printed commands, whether read silently or aloud, were badly executed. This test showed clearly that he found the same kind of difficulty in using numbers as we have already noticed with words.

(6) *Simple movements requiring no choice of right or left.* (See Table VI.):—

I gave him a series of simple commands, such as "Touch your nose," "Put out your tongue," &c.; these he carried out almost perfectly in response to words said by me. When, however, the order was given in print, which he read silently, his responses were faulty. Instead of closing his eyes he would touch one of them with his hand; told to give me his hand, he pointed with one of them to the other and rarely executed correctly the movement required. He read these orders aloud extremely badly and carried them out even worse than when he remained silent.

Asked to copy the printed sentences, their content was correctly given, but

TABLE VI.

	Printed commands	Oral commands	Reading aloud and executing printed commands		Copying and then executing printed commands	
			He said	Movement executed	He wrote	Movement executed
Shut your eyes ..	Touched R. eye with R. hand	Correct	"Shine . . you . . eye, eye." "Show . . eyes"	Did nothing	Shut youR eyes ..	Touched eye with hand
Give me your hand..	Pointed with R. hand to L. hand. "This isn't it"	,,	"Gee . . me . . you . . ann"	Touched L. hand with R.	Give Me youR hand..	Touched L. hand with R.
Touch your nose ..	"I think I know that word," pointing to nose. Did nothing	,,	"Too, too . . you . . no, now, new. New no"	Correctly	touch youR nose ..	Correctly
Put out your tongue	Did nothing	,,	"Pew . . two . . you . . toe." "I don't know what this is"	Did nothing	Put out youR tonGue	Did nothing
Give me your hand..	Touched L. hand with R.	,,	"Gee . . me . . you . . ann, fan, ann"	Touched L. hand with R.	Give me me youR hand	Touched L. hand with R.
Touch your nose ..	Correct ; very slow ..	,,	"Chew . . you . . no, nose"	Correctly	touch youR nose ..	Correctly
Put out your tongue	"Was it toe?" Did nothing	,,	"Pew . . no, no . . you . . tow"	Did nothing	Put out youR TonGue	Did nothing
Shut your eyes ..	Touched R. eye with R. hand	Touched R. eye with R. hand	"Show, shoud, shout . . you . . eye, eye"	Touched R. eye with R. hand	Shut youR eyes ..	Touched R. eye

the writing was a curious mixture of cursive script interspersed with irrelevant capitals. Although the actual words as written contained the correct commands, they were carried out extremely badly.

(7) *Hand, eye and ear tests* :—

TABLE VII.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Pictorial commands	Pictorial commands reflected in a mirror	Oral commands	Printed commands
L. hand to R. eye	R. hand to R. eye	Correct	Reversed	Correct	Lifted L. hand	R. hand to R. eye
R. hand to R. ear	Reversed	,,	,,	,,	Correct	R. hand . . .
R. hand to L. eye	R. hand to R. eye	,,	,,	,,	L. hand to L. *ear*	R. hand to R. eye
L. hand to R. ear	L. hand to L. ear	,,	L. hand to L. ear	,,	L. hand to L. ear	R. hand . . .
R. hand to R. eye	Correct	,,	Reversed	,,	Correct	Reversed
L. hand to L. ear	Reversed	,,	,,	,,	L. hand to R. ear	No response
L. hand to L. eye	,,	,,	,,	Reversed	L. hand to L. *ear*	Reversed
R. hand to L. ear	,,	,,	,,	Correct	R. hand to R. *eye*	L. hand to L. eye
L. hand to R. eye	R. hand to R. eye	,,	,,	,,	R. hand to R. eye	R. hand to R. eye
R. hand to R. ear	Reversed	,,	,,	,,	R. hand to R. *eye*	Reversed
R. hand to L. eye	R. hand to R. eye	L. hand to L. eye	,,	,,	L. hand to L. eye	L. hand to L. eye
L. hand to R. ear	L. hand to L. ear	Correct	L. hand, then R. to L. ear	R. hand to R. ear	L. hand to L. ear	L. hand to L. ear
R. hand to R. eye	Correct	,,	Reversed	Correct	L. hand to R. eye	L. hand to R. eye
L. hand to L. ear	L. hand to R. ear	,,	,,	,,	Correct	L. hand to R. ear
L. hand to L. eye	Reversed	,,	,,	,,	Reversed	L. hand . . .
R. hand to L. ear	,,	,,	R. hand, then L. to R. ear	R. hand to R. ear ; then L. to R. ear	R. hand to L. *eye*	Reversed

This series of tests brought out the same difficulties in an exaggerated form. He could not imitate my movements when we sat face to face, nor could he carry them out correctly from pictures. When either my movements or the diagrams were reflected in a mirror, his responses were not only much quicker, but he made four mistakes only in the double series of thirty-two observations.

As with all tests of this order, he found great difficulty in executing oral and printed commands and occasionally failed to complete the movement or mistook ear and eye.

Condition in July, 1922, *four years and nine months after he was wounded.*

The wound was represented by a tough arrow-shaped scar, lying over a triangular opening in the bone; this was depressed and in normal circumstances did not pulsate. But if he lowered his head towards his knees, the surface came up flush with the scalp and pulsation occurred. The skin did not seem to be tender in the true sense of the word, although he intensely disliked anything to touch this part of his head and was evidently frightened at the prospect of contact.

He complained of occasional "headaches" in the morning, which disappeared an hour or so after getting up. Stooping or lifting brought on this feeling, which was more a discomfort and sensation of "dizziness" than an actual pain. It could also be induced by reading or intellectual concentration. He had suffered from no fits or other attacks. The discs were normal; vision was perfect and there was no limitation of the field. All reflexes, including the abdominals and plantars, were normal. There was no paresis, inco-ordination, or change in tone, and sensibility was in no way affected. In fact, I could discover no abnormal physical signs of any kind. His general health was excellent.

Symbolic Formulation and Expression.

He had returned to his occupation as a music hall singer, but recently lost his engagement because his voice had deteriorated, and he was about to return to manual work.

Articulated speech.—He was somewhat nervous and anxious, speaking little except when in quiet and familiar surroundings. He said "I'll tell you what I'm most afraid of . . . I can't speak much in company . . . I get nervous and it stops me from speaking . . . I get confused . . . the words." To my question whether he knew what he wanted to say, he replied, "Yes, Doctor . . . but if they speak quickly I get taken off what I wanted to say."

He said the months correctly in order and had regained his power of naming common objects or colours, although he occasionally hesitated before replying. He had no difficulty in word formation, once he knew what he wanted to say; if he failed to find the correct expression, he did not stutter and make repeated attempts at articulation, but paused as if lost. Syntax was entirely unaffected and he showed no tendency to employ true jargon.

He could repeat everything said to him accurately and without verbal distortion.

Understanding of spoken words.—Common objects or colours were chosen rapidly without error to oral commands and he set the hands of the clock correctly. He made no mistakes even with the complex hand, eye and ear tests, although his choice was somewhat slow and hesitating. His appreciation of the significance of general conversation was excellent, provided I did not speak too rapidly, or talk of some entirely unfamiliar subject.

Reading.—He evidently understood what he read to himself, choosing common objects or colours and setting the clock correctly to printed commands. Even the hand, eye and ear tests were executed without mistakes to orders given in print.

He read aloud the phrases of the man, cat and dog tests with ease. But, when reading from a book, he occasionally hesitated at some unusual word saying, "I can say the names . . . unless they might be . . . big words . . . big names . . . or I can say them all if I have a good look at them . . . read them over . . . have a good look at them and say them over."

Writing.—He wrote his name and address perfectly and produced the following excellent letter, marred only by the insertion of irrelevant capitals.

"Dear Sir, I feel much better than I was, four years ago. In fact I feel Better in every way, of course I feel a Little Depressed at times, but it is nothing. Well I cannot write much, and it also takes me a Long time to do it

Yours faithfully

A. McN."

Designation in writing was still somewhat slow, although he could execute all the serial tests with few if any faults. Thus he found some difficulty with the names of common objects, but made no mistakes except with the spelling of knife and scissors. Colours were given correctly, he wrote the phrases of the man, cat and dog test accurately, and even put on to paper the complex hand, eye and ear movements without mistakes. The months were written in due order and February alone was wrongly spelt (Febuary), a trivial fault.

He wrote well to dictation and copied excellently keeping his eyes fixed on the printed matter before him.

The alphabet.—In spite of his extensive recovery of speech he experienced profound difficulty with this test. He had reached a high standard at an elementary school and said, "I was a good scholar before I was wounded." Asked to say the alphabet he began "A B C D E F G . . . "; he ceased and started again, "A B C D E F G H . . . ." Then he said "I can say the end of it, I L M N O P Q W X Y Z . . . there is one or two . . . letters . . . there . . . I'm not sure of." Yet he repeated the letters after me and read them aloud perfectly.

Told to write the alphabet spontaneously, he produced the following: a b C D E F G H L O P Q R S T U V W X Z; and to dictation he wrote a b C D E F G H I J K L M N o p q R S T W V W x v z (y troubled him greatly and was left unfinished). Given a series of capitals and asked to copy them in ordinary handwriting, he did so as follows: a b c D E F G H I J K L m n o p q R S t u v w x y z.

I then placed on the table the twenty-six block letters and asked him to make an alphabet; he completely failed to do so. He first ranged in order A B C D E F G I then exclaiming, "I think I've done it wrong" he removed the I and added H I. After much hesitation he continued L M N O P U R S T and then gave up altogether.

Thus, in spite of the profound recovery of speech, this test still revealed gross lack of power to manipulate verbal symbols.

Numbers and arithmetic.—He counted perfectly up to 69, but hesitated at 70; he then continued, "71, 72, 73, 74 . . . 70, 71, 72, 73, 74, 75," and so on correctly up to 100. Each number was considered separately and uttered individually, and not as part of a series.

Addition			*Subtraction*		
123	228	345	685	752	821
214	734	868	342	536	467
337	962	1,213	343	236	474
				(wrong)	corrected spontaneously to—
					354

Coins and their relative value.—All forms of money from a pound note downwards were correctly named and the relative value of any two of them was given slowly but accurately. He added, "I used to be awful . . . I couldn't count the change . . . not correctly . . . It is much better . . . now and again I make mistakes . . . if I try to do it quick I make mistakes."

Drawing.—He drew a spirit-lamp excellently from a model and reproduced it fairly well from memory. He was also able to draw an elephant with all its salient points, naming them correctly as he added each one to his drawing.

Pictures and images.—He showed perfect recognition of the full significance of pictures and carried out pictorial commands without fail.

When drawing the elephant, he insisted that he could see it "in my mind." Asked what colours I had shown him on the previous day, he gave them all correctly and added, "I can see them . . . see them all."

Orientation and plan-drawing.—During his stay in London he found his way about alone, came to my house from the Hospital unattended, and showed no signs of defective orientation.

Asked to draw a plan of the room in which we worked, he was much puzzled as to the relative position of the various objects and tended to draw them in elevation instead of indicating them on the flat. When, however, I drew a four-sided outline figure to represent the room and asked him to point to each object in turn as I named it, he did so with complete accuracy. It was the power of formulating the relation of the various pieces of furniture to one another which was at fault.

Games.—He could play billiards and draughts, but not cards; they had always given him trouble, since he was wounded, and he had not attempted to relearn these games.

Singing.—He could never read musical notation sufficiently to help him with his songs and learnt them all by ear. He still sang well without words; his voice had its full volume and showed no unsteadiness. But as soon as he attempted to sing the words of a song, he fell out of tune, the volume of his voice decreased and a bad tremolo made its appearance. Evidently the words hindered him, and he complained, "It's the words that worry me . . . better without words."

Serial Tests.

(1) *Naming and recognition of common objects.* (See Table VIII.) :—

Oral and printed commands were executed without the slightest difficulty, and he named the various objects correctly, although with occasional hesitation;

TABLE VIII.

	Pointing to object shown	Naming an object indicated	Oral commands	Printed commands	Duplicate placed in hand out of sight	Writing name of object indicated
Knife	Correct	Correct	Correct	Correct	Correct	Knike
Key	,,	,,	,,	,,	,,	Correct
Penny	,,	,,	,,	,,	,,	,,
Matches	,,	,,	,,	,,	,,	,,
Scissors	,,	,,	,,	,,	,,	Siccors
Pencil	,,	,,	,,	,,	,,	Correct
Key	,,	,,	,,	,,	,,	,,
Scissors	,,	,,	,,	,,	,,	Siccors
Matches	,,	,,	,,	,,	,,	Correct
Knife	,,	,,	,,	,,	,,	,,
Penny	,,	,,	,,	,,	,,	,,
Matches	,,	,,	,,	,,	,,	,,
Scissors	,,	,,	,,	,,	,,	Siccors
Pencil	,,	,,	,,	,,	,,	Correct
Penny	,,	,,	,,	,,	,,	,,
Knife	,,	,,	,,	,,	,,	Nife
Key	,,	,,	,,	,,	,,	Correct
Pencil	,,	,,	,,	,,	,,	,,

but his lips did not move, even during the moments of doubt. Told to write down the name as each object was shown to him, the nomenclature was correct, but the spelling of scissors and knife defective.

(2) *Naming and recognition of colours.*—All these tests were carried out perfectly and the names were even written without mistakes. This shows the profound extent to which he had recovered power to use language in its various forms.

(3) *The man, cat and dog tests.*—He read aloud from print or pictures and repeated these phrases perfectly. He could write them from pictures or to dictation and copied print in ordinary handwriting without mistakes of any kind. In fact, he said that these tests gave him no trouble.

(4) *The clock tests.*—He set the clock to oral and printed commands, placing the short hand throughout in a position proportionate to the minutes indicated. He told the time perfectly and wrote it down without mistakes, adding, "It seemed to come to me all of a sudden, when I got home first . . . I seemed to read the clock."

(5) *The coin-bowl test.*—This gave him no difficulty and all the tests were executed rapidly and well.

(6) *Hand, eye and ear tests.*—These showed in a striking manner the profound recovery of power which had occurred since he first came under my care. He not only imitated my movements sitting face to face, but carried out oral, printed or pictorial commands correctly, though somewhat slowly. When my movements or the pictures were reflected in a mirror, his response was much quicker. He could even write down without mistakes my movements sitting face to face, or those indicated in the diagrams, a task of considerable difficulty even for a normal person.

During the course of these tests he volunteered the following statements: "I looks at your arms . . . then I . . . . well I looked at your right arm or your left . . . and that kind of tells me . . . I say it." "It's difficult if it's quick . . . when I do it quick . . . I don't think I'll do it correctly."

At first this patient showed profound loss of power to find names and the indicative words he required to express his thoughts. He could not carry out oral or printed commands and was unable to write although he could copy. In the course of somewhat over four years, he recovered his power of speaking, reading and writing sufficiently to carry out all the serial tests, excepting only those set by the alphabet. But it was obvious that he still had difficulty in naming, and the more complex oral and printed commands were executed with abnormal deliberation. In fact, he still remained an example of nominal aphasia, in spite of the remarkable restoration of the power of speech in all its forms.

§ 5.—*A Case of Semantic Aphasia, due to a Wound with a Hand-grenade in the left Supra-marginal Gyrus. Observations, extending over seven years, showed considerable variation in the degree, but not in the character of the disturbance of function.*

No. 10.—Lieutenant Robert M., who was an accountant before the War, enlisted in September, 1914, obtaining his commission in June, 1915. At the time of his wound he was 32 years of age and a most intelligent Scotchman.

He was bombing officer to his regiment, and on March 17, 1916, during a course of instruction to his men on the use of hand grenades, he was wounded accidentally. He remembers nothing of the occurrence, or of anything that happened on that day.

He was admitted to hospital at le Tréport on March 18, with two small wounds over the left parietal area, which affected the brain, together with scattered injuries of little import over the chest, abdomen and arms. He was semi-conscious and rambled in his speech. The pupils were equal and reacted to light. There was no paralysis.

On March 18 he was trephined; on enlarging the openings the dura mater was found to have been perforated in two places and two small fragments of depressed bone were removed. A small drainage tube was inserted through each opening into the brain. These were removed on March 22, and his progress was reported to be satisfactory.

When admitted under my care to the Empire Hospital for Officers on April 20, 1916, there was a healed wound in the left parietal region. Bone had been removed over an oval area 2·5 cm. by 1·25 cm., extending from 15·5 cm. to 18 cm. along the nasion-inion and 8 cm. to the left of the middle line. The total distance from nasion to inion was 34 cm. The wound was firmly healed and did not pulsate (cf. figs. 6 and 7, pp. 410 and 411).

On physical examination, I could find no abnormal signs of any kind except the disorders of speech. His vision was R. $\frac{6}{6}$, L. $\frac{6}{9}$, with slight myopia. The visual fields were not restricted and the discs showed no changes. Motion, sensation and the reflexes were unaffected.

He was a strongly right-handed man, who could neither throw, nor cut left-handed with the loose-jointed scissors (Gordon's test). He could tie a reef-knot and had no difficulty in using knife, fork, spoon or other tools. He made the movements of brushing his hair without a brush in his hand and could pretend to take a cigarette from his case, strike a light and blow it out again.

He had not suffered from fits or any other attacks. His headache varied greatly; it was never acute or associated with nausea and vomiting, but was "dull" and diffused mainly on the left half of the head. It was greatly increased by fatigue and concentrated mental effort. He was conscious of an abnormal sensation when he stooped to do up his boots, but not with less extreme changes of posture. Once induced, the headache required some days before it passed away.

Condition of Symbolic Formulation and Expression in May and June, 1916, *ten weeks after he was wounded.*

He was a remarkably intelligent man and a most willing subject for examination. His temper was unusually equable, even when he found difficulty in expressing himself, and he was bright and happy throughout his stay in the hospital.

Articulated speech.—He had no difficulty in finding or articulating words to express his ordinary needs and all his phrases were perfectly formed and spaced. Syntax was entirely unaffected. But in general conversation he paused like a man confused, who had lost the thread of what he wanted to say.

He could say the days of the week and months correctly and counted without hesitation or error.

He had no difficulty in repeating anything said to him, provided the sentence did not contain a number of possible alternatives; any mistake he might make depended on faulty comprehension or memory, and not on want of power to repeat what was said.

Understanding of spoken words.—At first sight he appeared to understand all that was said to him, choosing both geometrical shapes and colours correctly, though with some hesitation to oral commands. But with the more complex clock tests he failed lamentably, evidently unable to comprehend the full significance of the order. His response to the hand, eye and ear tests were even worse; eye and ear were confused and he tended to fail in executing an order which required him to bring his hand across to the opposite half of the face. Moreover, in general conversation he was liable to become confused, because he did not understand the full meaning of what was said.

This he explained as follows: "I don't seem to understand all you say and then I forget what I've got to do."

Reading.—He could understand the significance of printed words and short sentences without fail, provided they did not contain a command. But, when asked to read silently to himself a series of paragraphs in the newspaper, he gave a poor account of their full meaning; he lost the thread of what he wanted to say and his narration tailed away aimlessly.

He chose the following message from the King on the Battle of Jutland: "I am deeply touched by the message you have sent me on behalf of the Grand Fleet. It reaches me on the morrow of a battle, which has once more displayed the splendid gallantry of the officers and men under your command. I mourn the loss of brave men, many of them personal friends of my own, who have fallen in their country's cause; yet even more do I regret that the German High Seas Fleet, in spite of its heavy losses, was enabled by the misty weather to evade the full consequences of an encounter they have always professed to desire, but for which, when the opportunity arrived, they showed no inclination. Though the retirement of the enemy immediately after the opening of the general engagement robbed us of the opportunity of gaining a decisive victory, the events of last Wednesday amply justify my confidence in the valour and efficiency of the fleets under your command."

After he had read it through to himself, he said, "The King refers to the loss of the many brave men under his command, many of them personal friends of his own. He refers to the loss of the many brave men. He lays great stress on the fact that the Germans were evidently unable. . . to come to grips . . . with our men."

He could read aloud simple sentences perfectly without mispronunciation; but in the course of a long or difficult passage he tended to become confused, even though he was reproducing the words correctly. Given the King's message, he read it aloud correctly until he reached "yet even more;" thence he continued in jerky sentences of a few words apiece until he came to "for which . . . they have always professed a desire . . . for which they have . . . they have the opportunity . . . arrive they show no inclination," when he stopped and said, "That's funny, I seem to be getting the wrong sense somehow. Shall I go on?" Encouraged to do so, he read to the end correctly.

He was then asked what he understood from the paragraphs he had read aloud, to which he answered, "You see, Doctor, it's like this; I've got a general epitome of what I've been reading in the paper. When I tell you, I may get it mixed up. About the King's message . . . The fleet was at the . . . If they hadn't had the opportunity to fully engage the German fleet . . . the, ah yes, misty weather spoilt things . . . notwithstanding our men's keenness to force a general action, the misty weather and the enemy's disinclination to fight robbed us of victory."

He had no difficulty in reading and understanding a letter written by himself or by others, provided it did not deal with matters which would have confused him however they had been presented.

Writing.—His handwriting was profoundly altered; he wrote his name and address with extreme rapidity, twice employing the peculiar letter like a 𝒬, which formed so prominent a feature of his script at this stage.

Asked to compose a letter to me, he wrote as follows, saying the words aloud: "Dear Dr. Head, I have a vase containing some beautiful flowers. My wife brought me some lilies of the valley." At the same time he wrote with considerable difficulty a scrawl which was comprehensible only if his intention was known. This he read aloud exactly as if it had been perfectly written. Throughout he showed a peculiar tendency to use a figure resembling 𝒬 for D F O R T and V.

I dictated to him, "The lilies of the valley, which are standing on my table, were sent to me by my wife from Cork." This he wrote with difficulty; he dashed off the first few words, paused, and suddenly wrote "which are standing on my table," and then stopped. I repeated several times, "which were sent me by my wife" before he could put the next phrase on to paper, and even then he omitted "wife"; and yet he read what he had written exactly as if it were a perfect reproduction of the sentences I had dictated.

He could copy the names of the colours from print, but wrote extremely rapidly and tended to employ the curious sign 𝒬 in place of several of the initial letters. Asked to copy the simple man, cat and dog phrases, he tended to reproduce a common fault, which ran throughout these tests, substituting in this case "man" for "cat."

The alphabet.—He could say the alphabet perfectly and repeat it without fail. But, when asked to write the letters, he said each one aloud once or more and wrote the above script (fig. 10). He added, when he had finished, "I seem to get mixed between capitals and other letters." To my dictation he produced an almost identical alphabetical sequence.

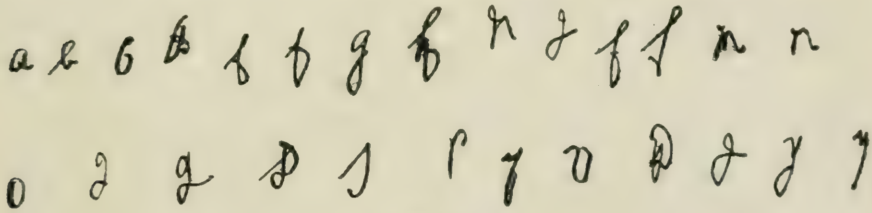

FIG. 10.

General significance of pictures and print.—Shown a picture and asked to describe what he saw, he went over it in detail, usually beginning at one side and working across to the other: but, as a rule, he failed to appreciate its general significance. For instance, he was shown a photographic reproduction of the tower with the leaning Virgin at Albert; at the top of the picture was printed, "When the end of the war will be; a prophecy." After examining it with care and reading the superscription, he said that it reminded him of something he had seen before; "In the other picture I saw, there was a piece of statuary. I don't know if that is a confusion in my mind or not. It was a piece of old building tumbling down; like the leaning tower of Pisa. That building has fallen over much more than this; the local French people believe that the statue of the Virgin Mary . . . they believe that the statue has fallen and that then the war will end . . . just in that place the war will end." During the narration he looked away from the picture, evidently recalling some previous memory, and I therefore said: "What bearing has this picture on the story you have just told me?" He then looked at the picture again, passing his finger over the various details as he mentioned them. "This is simply a building, that has been bombarded, in ruins; one tower, as often happens, seems standing unmolested. I can now see the statue quite plainly; I can see the arms quite plainly. I think I might have been confused about the statue if hadn't known the story." It was not until after he had recounted to me the familiar legend and recalled previous illustrations he had seen of the church at Albert, that he suddenly noticed the most salient feature in the picture before him.

In consequence of this difficulty in recognizing the full significance either of pictures or of printed matter, most jokes were incomprehensible. Suppose, however, that the humour consisted solely in the detail of the drawing, it might be appreciated; but any demand for co-ordination between its various parts, or with the text beneath it, met with little response.

I showed him a drawing from one of the comic papers where the point depended on the appreciation of the significance of summer-time, then a much discussed novelty. Standing beside a clock, whose hands pointed to two, the bride of a day says to her bridegroom: "Look, it's 2 o'clock, and yesterday at this time it was 1," and he replied: "Yes, darling; and yesterday at this time we were two, and now we are one." The patient remarked: "I've got the drift of that. It's not much of a joke. They've stupidly been married; the bridegroom has something stupid to say about yesterday we were two and now we are one." Then, pointing to the clock, he said: "I could have told the time there better than when you were trying me . . . two o'clock." I asked: "What happened at two o'clock, just a fortnight ago?" He replied: "Oh! I see, Daylight Saving Act." To my question, "What happened to the clocks?" he answered: "They were put back an hour. That's a thing I'm rather hazy about. I have to think of that . . . forward . . . back, no, I have to give that up; I've been trying to think that out, and haven't got to a conclusion yet, somehow."

Then I told him "The clock was put forward; at twelve o'clock it was put forward to—— ?" and he replied: "Put forward . . . well at twelve o'clock it was put forward to half-past eleven. I shouldn't think it was half an hour, anyhow; half-past eleven, no, eleven o'clock. I can't get it; I seem to have got the idea, but I can't get hold of it."

General intention of an act to be performed.—This inability to grasp the general significance or intention of an act he is asked to perform was well illustrated during the tests for the spacial aspects of sensation. When the index finger of either hand was moved passively, even with the eyes open, he did not give consistently appropriate replies. Sometimes he said correctly "the same," "two together" (for two movements in the same direction), "different," "not the same;" or if I asked: "Which way is it moving?" he would answer "forwards," "backwards," "bending," or "straightening." But, if I remained silent, he usually simply replied "yes," or wagged the finger of the other hand aimlessly backwards and forwards without indicating the direction.

If, during the compass tests, he was touched with a single point more than once successively, he tended to count "one," "two," "three"; then he would exclaim: "Oh! bother I've muddled it again." Although sensation was unaltered, he could not hold fast in his mind that the intention of the test was to determine his power of discriminating contact with one or two points.

Asked to point to the spot on either hand touched by me, he did so without difficulty; but, unless the command was repeated every time, he would forget what he had to do and held the indicating finger poised in the air. If I repeated the order he would exclaim "Oh! yes, of course," and carry it out correctly.

His power of appreciating the addition or removal of weights placed on the palm of either hand was certainly unaffected. But he frequently failed to give a consecutive reply, saying "I don't know what you mean by on and off; I get confused"; and yet on more than one occasion he volunteered the statement "You touched the weight, you did not take one off," which was quite correct. I laid two weights on the table in front of him and requested him to place one on to the other, or to take it off silently, in order to indicate whether I had added or removed a weight from his hand. This confused him profoundly and he made no attempt to carry out the command, although he had been previously answering correctly by word of mouth.

Arithmetic.—Although he counted excellently and with ease he was entirely unable to carry out the simplest arithmetical operation. He could not even add 231 and 356 or subtract 432 from 865. He said "I seem to get tangled up in the process." This is the more remarkable as he was an accountant in civilian life, accustomed to handle complex masses of figures.

Coins and their relative value.—He named every coin with perfect ease. But, as soon as two of them were presented to him and he was asked, "How many of this one (of lower value) go into this one (of higher value)?" he became confused. The following are some of his answers:—

A penny and sixpence	"Twelve"
Sixpence and a shilling	"Twelve . . . . yes, twelve, sixpence"
Sixpence and half-a-crown	"Let me see, twenty-two . . . I thought of twenty-four, but it's not"
A halfpenny and a penny	"Penny and halfpenny, penny and two pence . . . . no, penny and halfpenny"

A halfpenny and sixpence ...	"Six and twelve is it? . . No"
One penny and a shilling... ...	"Twelve"
Sixpence and half-a-crown ...	"Six . . . . twenty-four"
Sixpence and one shilling ...	"Six . . . . twelve"
One penny and sixpence	"Twelve"

Drawing.—He was unable to delineate a vase of simple form either from the model or from memory. Asked to draw an elephant, he failed entirely to produce a figure of any kind, but scrawled idly on the paper.

Plan-drawing and relation of objects in space.—Told to draw a plan of his room in the hospital, he failed entirely; he made no attempt even to put the pencil to paper, saying: "I've all sorts of ideas, but I can't carry them out."

But, with his eyes closed, he had no difficulty in pointing to the position of the window, fireplace, washhandstand, chest of drawers and other pieces of furniture. When asked to say how the washhandstand stood in relation to the fireplace, or the latter to the door, he entirely failed to do so; allowed, however, to say: "The fire is there and the door there," he pointed to their position with complete accuracy. He knew exactly where they were and was certain that he could "see them in his mind," but was unable to express their relative position to one another.

Orientation.—He was extremely liable to lose his way in the hospital and had difficulty even in finding his room. This feature of his affection was more fully investigated when he was up and about, and is considered more in detail later.

Games.—He could play no games such as chess, draughts or cards; nor could he put together "jig-saw" puzzles, so popular an employment amongst wounded soldiers.

Serial Tests.

(1) *Naming and recognition of common objects*:—

TABLE I.

	Pointing to object shown	Oral commands	Printed commands	Duplicate placed in hand out of sight	Naming an object indicated	Writing name of object indicated
Cylinder ..	Correct	Correct	Correct	Correct	"The cube"	C
Cone ..	,,	"A cone and a pyramid: but I can't." Correct	,,	,,	Correct	Wrote nothing
Cube ..	,,	Correct	,,	,,	,,	C
Sphere ..	,,	,,	,,	,,	,,	Sp
Ovoid ..	,,	,,	,,	,,	,,	O
Pyramid ..	,,	,,	,,	,,	,,	𝒬
Sphere ..	,,	,,	,,	,,	,,	Sp
Cone ..	,,	"Pyramid; no." Chose correctly	,,	,,	,,	Clo
Ovoid ..	,,	Correct	,,	,,	,,	𝒬 ov
Cube ..	,,	,,	,,	,,	,,	Scrawl
Cylinder ..	,,	,,	,,	,,	,,	Wrote nothing
Pyramid ..	,,	,,	Chose cone; then correctly	,,	,,	Sype

During the observations on sensibility I found he was unusually accurate in his nomenclature of geometrical figures, and I therefore selected them as the objects to be named or indicated in this test. With the general run of patients the names applied to these solid figures are so inconstant and uncertain, that it is not advisable to use them in this manner ; but in this case they distinctly added to the value of the results obtained.

He showed little difficulty in pointing to an object named orally or in print and made one mistake only in nomenclature. But he failed entirely to write their names ; he not infrequently hit upon the correct initial letter, although he showed a tendency to use the same symbol for different capitals.

When he was told to say each name aloud before putting it into writing, he did so correctly ; but he produced an illegible scrawl which, however, contained the same number of signs as the word he had uttered. For instance, he said "Cylinder yes, C.Y.L.I.N.D.E.R," and as he spelt each letter he made a mark upon the paper, which might or might not correspond to its normal shape. "Pyramid" was correctly articulated ; but he then said "P.Y.R.I.M.D" and wrote a word consisting of six more or less incomprehensible letters.

(2) *Naming and recognition of colours* :—

TABLE II.

	Pointing to colour shown	Oral command	Printed commands	Naming	Writing name of colour indicated	Copying names from print	Printed name read aloud and colour chosen	
							He chose	He said
Blue ..	Correct	Correct	Correct	Correct	𝒬lue	𝒬lue	Correct	Correctly
Yellow ..	,,	,,	,,	,,	Orange	𝒬ellow	,,	No choice
Red ..	,,	,,	,,	,,	𝒬ed	𝒬ed	,,	Correctly
Black ..	,,	,,	,,	,,	𝒬lack	Black	,,	,,
Orange ..	,,	,,	Yellow	Red	Orange	𝒬range	,,	Yellow
White ..	,,	,,	Correct	Correct	Whide	White	,,	Correctly
Violet ..	,,	.. (slow)	,,	,,	𝒬iolet	𝒬iolet	,,	,,
Green ..	,,	Correct	,,	,,	𝒬reen	𝒬reen	,,	,,
Blue ..	,,	,,	,,	,,	𝒬lue	𝒬lue	,,	,,
Yellow ..	,,	,,	,,	,,	𝒬range	𝒬ellow	,,	Green
Red ..	,,	,,	,,	,,	𝒬ed	𝒬ed	,,	Correctly
Black ..	,,	,,	,,	,,	Black	Black	,,	,,
Orange ..	,,	Yellow	Yellow	Red	𝒬range	𝒬range	,,	Yellow
White ..	,,	Correct	Correct	Correct	White	White	,,	Correctly
Violet ..	,,	,,	,,	,,	𝒬iolet	𝒬iolet	,,	,,
Green ..	,,	,,	,,	,,	Green	Green	,,	,,

Asked to point to a colour corresponding to one he had been shown, he answered correctly, but tended to forget the order in which they lay on the table before him. He swept his finger backwards and forwards along the row until he found the one he wanted ; then he answered without doubt or hesitation.

Printed commands were carried out somewhat more easily than those given orally, though both were on the whole correctly executed; the choice of yellow for orange can scarcely be reckoned as a mistake. When he attempted to name the various colours, he responded quickly and with assurance, but made three errors, twice calling orange "red" and once saying "orange" for yellow.

Told to write these names, he produced in each case something, which distinctly represented the colour shown to him, although the letters were badly formed and there was a peculiar tendency to use a common sign for B G R V and Y.

When he was asked to copy these names from print, he almost exactly repeated his previous performance; to write words evoked on seeing a colour and to copy them from a card seemed in this case to be an almost identical task.

(3) *The man, cat and dog test*:—

TABLE III.

	Reading aloud	Reading from pictures	Writing from pictures	Writing from dictation	Repetition	Copying print into handwriting
The dog and the cat	Correct	Correct	Dog and Cat	(illegible word) the Cat	Correct	The Dog and the Cap asp
The man and the dog	,,	,,	Man and "No, I'm done"	The man and the Dog	,,	The man and the Dog
The cat and the man	,,	,,	Cap and man	The cat and the man	,,	The cat and the man
The cat and the dog	,,	,,	D Cap and "No, I can't"	The cat and the man	,,	The man and the Dog
The dog and the man	,,	,,	Dog and man	The 𝒟og and the man	,,	The Dog and the man
The man and the cat	,,	,,	Man and cat	The man and the cat	,,	The man and the cat

He had no difficulty in reading from print and from pictures or in repeating after me the series of short sentences of which this test is composed.

But his writing showed the same peculiar changes noticed with previous methods of examination. He wrote with extreme rapidity, as if afraid of forgetting what he intended to do. Thus, when the pictures of the dog and the cat were placed before him, he gazed at them for a time; suddenly he exclaimed, "I've got it," dashed off "dog and," paused and then added a scrawl to represent "cat." Shown the man and the dog, he wrote "man and," adding "now I'm done." Writing from dictation seemed to be equally uncertain and was carried out at extreme speed. Even copying showed the same peculiarities; thus, when a card bearing "the dog and the cat" was laid before him he wrote rapidly "the dog and the," paused, added "cap," said "No, that's not it . . . cat," wrote "asp" and finally gave up, saying "No, I can't do it."

(4) *The clock tests*:—

TABLE IV.

	Direct imitation	Oral commands	Printed commands	Telling the time	Writing down the time	Telling the time and writing it down at once		Copying print in handwriting
						He said	He wrote	
5 minutes to 2 ..	Correct	Set 2.10	Both hands at 2	Correct	Wrote nothing	Two o'clock . . . about two o'clock	Qwo o'clock	Correct
Half past 1 ..	,,	Set 1.10	Both hands at 1; "I seem to think there is something wrong."	,,	Correct	Correct	Correct	,,
5 minutes past 8 ..	,,	Both hands at 8	Both hands at 8	,,	Ten minutes past eight	,,	,,	Ten past eight
20 minutes to 4 ..	,,	Both hands at 4; then 4.25	Long hand at 4; short hand at 7	Twenty-five minutes to four	Gave up	Twenty minutes past seven	Twenty minutes past seven	Correct
10 minutes past 7 ..	,,	Long hand at 7; short hand at 5	Correct	Ten minutes past eight . . . seven	Correct	Correct	Correct	,,
20 minutes to 6 ..	,,	Set 6.20	Set 6.15	Twenty-five to six	Ten minutes past seven	,,	Twenty minutes to sis	Twenty minutes to sis
10 minutes to 1 ..	,,	Set 1.10	Both hands at 2	Five to eight . . . no, that's ten	Correct	,,	Correct	Correct
A quarter to 9 ..	,,	Correct	Correct	Correct	Quarter to eight	,,	,,	,,
20 minutes past 11	,,	Long hand at 11; short hand at 10	Long hand at 11; "I've no certain opinion"	Ten minutes past eleven. "I get confused between hour hand and long hand"	Ten minutes past four	Twenty past twelve	twenty minutes past twelve	twenty past ilfion
25 minutes to 3 ..	,,	Long hand at 3; then gave up	Set 3.35	A quarter past seven	Half past seven	Quarter past seven	Quartar past siven	Correct

Although he was able to reproduce exactly by direct imitation the position of the hands on a clock set by me, his method of action was clumsy. Thus, in order to place the minute hand at 45, he would move it all round the clock from 50, its previous position; to set 7.10 after 3.40, he moved both hands round to 7 and then swung the long hand to ten minutes past the hour. He did not appreciate quickly the relation of a task he had solved successfully to one he was about to perform.

Both verbal and printed commands were carried out with extreme difficulty and uncertainty. He failed to differentiate the symbolic value of the two hands and confused "to" and "past" the hour. Similar mistakes were apparent, when he attempted to tell the time, and still more when he wrote it down silently. If he was permitted to say it aloud before writing it, what he wrote depended entirely upon the words he uttered. Even copying from a printed card was imperfectly carried out.

(5) *The hand, eye and ear tests.* (See Table V.) :—

This series of tests puzzled him greatly and reading aloud the orders in print was alone executed correctly. Throughout all these other tasks, he tended to make the same kind of mistakes, confusing eye and ear, or right and left, failing in most instances to recognize that an order required him to bring his hand across his face to touch the eye or ear of the opposite side. Throughout all these observations, he moved his lips and occasionally could be heard to repeat the command, usually incorrectly. He complained "My initial difficulty seems to be right and left; it confuses me and I forget the rest of what I've got to do."

No wonder that, under such conditions, he failed to imitate my movements sitting face to face, or to carry out pictorial commands; for both require accurate appreciation and reproduction of a somewhat complex formula. But his uncertainty of general intention led him even to confuse these orders when reflected in a mirror; he failed to recognize that he had simply to imitate exactly what he saw in the glass without reasoning about right and left. Oral and printed commands were also badly executed and he could frequently be heard to repeat the order wrongly under his breath. This was not so much due to want of power to understand the actual words as to an inability to formulate and retain in his memory the general intention of what he was told to do.

Subsequent Progress.

So long as he remained in the Empire Hospital, where he occupied a room to himself, he progressed favourably. But, at the end of July, 1916, he was sent to our Convalescent Hospital at Roehampton. Here many of the patients were up and about, occupied in games and other more or less active amusements. There was a large camp close by in Richmond Park; bands played, men marched and the sound of explosions from the bombing school were distinctly audible. He wandered about unhappily and complained that there was "too much going on, it puzzles me. They are always going by with a band and I want to think what they are. It bothers me." He suffered

TABLE V.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Pictorial commands	Pictorial commands reflected in a mirror	Oral commands	Printed commands	Reading aloud printed commands
L. hand to R. ear	Touched chin with L. hand	Correct	L. hand to L. ear	L. hand to L. ear	R. hand to R. ear	Held up L. hand	Correct
R. hand to L. eye	R. hand to R. eye	R. hand to R. *ear*	L. hand to L. eye	Correct	Correct	R. hand . . "I couldn't follow so much"	,,
R. hand to L. ear	L. hand to L. *eye*	R. hand to R. ear	R. hand to R. ear	R. hand to R. ear	R. hand to R. ear	R. hand to R. ear	,,
L. hand to L. eye	R. hand to R. eye	Correct	R. hand to R. *ear*	Correct	Correct	Correct	,,
R. hand to R. ear	Correct	,,	Reversed	,,	,,	,,	,,
L. hand to R. eye	R. hand to R. eye	,,	R. hand to R. eye	L. hand to L. *ear*	L. hand to L. *ear*	R. hand to R. eye	,,
L. hand to L. ear	Reversed	,,	Reversed	Correct	L. hand to L. *eye*	L. hand to L. *eye*	,,
R. hand to R. eye	,,	,,	,,	R. hand to R. *ear*	Correct	No answer	,,
L. hand to R. ear	R. hand to R. ear	,,	R. hand to R. ear	L. hand to L. ear	L. hand to L. *eye*	L. hand to L. ear	,,
R. hand to L. eye	R. hand to R. *ear*	R. hand to R. eye	Reversed	R. hand to R. *ear*	R. hand to R. eye	R. hand to R. eye	,,
R. hand to L. ear	R. hand to R. ear	R. hand to R. ear	R. hand to R. ear	L. hand to L. ear	L. hand to L. ear	L. hand to L. ear	,,
L. hand to L. eye	Correct	L. hand to L. *ear*	Correct	R. hand to R. *ear*	Reversed	Reversed	,,
R. hand to R. ear	,,	Correct	Reversed	Correct	Correct	R. hand to R. *eye*	,,
L. hand to R. eye	R. hand to R. *ear*	L. hand to R. *ear*	R. hand to R. eye	L. hand to L. eye	L. hand to L. eye	L. hand to L. eye	,,
L. hand to L. ear	Correct	Correct	Reversed	Reversed	Reversed	Reversed	,,
R. hand to R. eye	,,	,,	,,	R. hand to R. *ear*	,,	Correct	,,

from headache, mostly over the left side, but nausea and vomiting were absent The discs were normal.

On *August* 23, 1916, he had definite epileptiform convulsion, which was seen by Dr. Riddoch, who was talking to him at the time. He ceased speaking, turned towards the right side; his eyelids closed. The right arm became flexed and rigid, but there was no clonus and the leg was not obviously affected. The conjunctival reflex was absent. He did not bite his tongue or evacuate urine or fæces. After the attack was over the right plantar reflex gave an upward response.

In *September*, 1916, he was moved back to the Empire Hospital for closer observation, and his general condition improved greatly under the influence of quiet and restricted surroundings. His headache almost disappeared and nausea and vomiting were absent. The discs were unaffected and visual fields normal. There was neither paralysis nor paresis, and all the reflexes, including the abdominal and plantar, were unaffected.

On *October* 16, 1916, Mr. Walton explored the wound. A small flap was turned down and an irregular trephine hole was discovered, filled with tough fibrous tissue. This was dissected away carefully and a small piece of bone (0·8 by 0·5 by 0·2 cm.) was taken away from the superficial part of the cortex. When the scar tissue was removed this fragment was visible without further dissection. The wound healed by the first intention.

He was sent to the country and his general condition greatly improved. All headache disappeared; he remained free from attacks and showed no physical signs of a lesion to the nervous system, beyond the condition of his speech.

In *June*, 1917, he was again put through a complete examination. The tests with common objects were now carried out perfectly and those of the man, cat and dog series were noticeable only for the extreme rapidity with which he wrote. He asked to be permitted to leave out the "thes" in writing, for "I keep track of it better" if allowed to shorten the sentence in this way. The clock tests still showed all the previous faults in executing oral and printed commands, and the results of the hand, eye and ear tests were almost identical with those set out on Table 5. He made the definite statement that, when attempting to carry out oral and printed commands, "I seem to act more spontaneously, but I still say it over to myself. Though I don't say it aloud, I say it to myself." If he was permitted to say it aloud his actions were almost perfectly in accord with the order given by word of mouth or in print.

He could write an excellent letter, but had extreme difficulty in reducing the alphabet to writing. In the course of what he wrote spontaneously in my presence, occurred the following passage, "Shall I now try to tell you of a very Diffcul tast you set me, that is trying to write the Letters of the alphabet. This test is one which I always felt would be Difficut. he trouble is mostly in beginning the Letters i.e. actual Letters of the alphabet wihle I can write straight on beginnin a new letter or sentence troubles me. This may not be very intellegible to you, but if I may, I shall try to explain my somewhat rambling . . . ." He then ceased and appended his signature. He had no difficulty in reading this whole letter, when written ; he appreciated where he had gone wrong and corrected some of the mistakes.

Arithmetical operations were impossible, except the first or simplest addition and subtraction sums. He had no difficulty in naming coins, but was still slow in recognizing their relative value, though his answers were on the whole correct.

He was given a brightly coloured picture of a jetty with a small lighthouse projecting into the sea ; moored close to shore was a fishing boat that filled up at least one-third of the picture. Holding it in his hand he began to describe what he saw : "It's a picture of the sea . . . and it shows the harbour and . . . the . . . this might be a light house . . . and there's a steamer out at sea . . . Life boat, on rollers ready for launching . . . there's a small boat here [pointing to the shore]. There's a ship here possibly for pulling up any sort of boat." He entirely missed, in this detailed description, the large fishing boat, which filled up a considerable portion of the picture. After it was removed he again enumerated from memory the various objects he had seen, entering into even closer detail. The picture was then replaced in his hands and he suddenly exclaimed, "Oh ! I left out the very large boat, fishing boat, sailing boat. I think I missed it from the beginning."

After an attack of influenza in *July*, 1918, he regressed and did not recover his powers of speech, up to the point he had previously reached, until the beginning of 1919. In March of that year his condition was much the same as that I have just described, but by June he showed distinct improvement.

I pass over all my observations during the next two years, which simply confirmed and amplified those already recorded.

Condition five years after the Injury (*April* 28 *to May* 4, 1921).

He was in splendid physical health and did not suffer in any way from his head. But he complained that he easily became tired especially if he had to think much and then lost "the grip of things." "If I've got to hurry it puts me out directly."

He had been through a course of training in apiculture under the ægis of the Pensions Ministry. His wife, an extremely able young woman, took part in this instruction, and it was she who managed all the business and administration, whilst he carried out the physical work required for the industry.

Articulated speech.—He could find all the words and names he required for daily use ; his sentences were perfectly formed and spaced and syntax was unaffected ; but he still showed a tendency to become confused in the give and take of conversation. He was able to say the days of the week or the months correctly and counted without mistake or hesitation. Repetition was perfect, provided the phrases were not long and complicated in their significance.

Understanding of spoken words.—On superficial examination he seemed to understand all that was said to him. He had no difficulty in choosing familiar objects or colours to oral commands, but he failed grossly to set the hands of the clock, or to carry out the hand, eye and ear tests, to orders given by word of mouth.

In ordinary intercourse he was frequently unable to comprehend with uniform exactitude what he had heard and so became easily confused. Of this several characteristic instances are given below.

Reading.—He still had profound difficulty in grasping the full significance of what he read silently, although he could read aloud without mistakes and with perfect enunciation (*vide infra* p. 513).

Writing.—He wrote with undue rapidity and formed his letters carelessly, as if in fear that he might forget what he intended to express. But his script was now legible and he had ceased to employ a common sign for several different capital letters.

The following excellent letter was composed and written spontaneously in my presence : " Dear Dr. Head, London seems very beautiful at present. The trees look so fresh and green that one might almost imagine oneself in the country. Nearly two years ago I was in London and was very much impressed by the beauty of the trees. London must, I think, look at its best in early May. My mother visited London at Easter and was full of enthusiasm for the natural beauty of the surroundings, the blossoms on the fruit trees particularly taking her attention. I do not mean to say that London is more beautiful than the country—it is very beautiful in some respects wonderfully so—but what seizes the imagination is that so much beauty should exist around a great city. The cause may, I should say, be given in one word—trees."

Here the only faults were poor handwriting and careless spelling, corresponding to the hurried manner in which he carried out his task. He read this letter over aloud to me perfectly and did not notice any of the mistakes.

He could write to dictation and copy correctly, but his handwriting tended to show the same faults as when he wrote spontaneously.

The alphabet.—He could say, repeat and read aloud the alphabet in perfect order, quickly and without mistakes.

But, when he came to write the letters, he lost the thread in the middle ; he paused after J, started again with I, and then, except for two illegible scrawls before L, wrote the remainder correctly. To dictation he made the same sort of mistakes, writing mainly in capitals : 𝒜ℬ CD ℰℱ𝒢 H 𝒥ℐ𝒥 𝒦ℒ *m n* O 𝒫𝒬 R 𝒮𝒯 *u v w x y z.* When I said G he wrote "*J*," and followed it rapidly by "*G*" in response to a second command ; but for I, he again substituted "*J*," correcting it on repetition of the order. He was then asked to copy the printed alphabet : this he carried out in cursive handwriting, slowly and with evident difficulty. For *k* he first wrote "*h*" and added "*k*" ; r was preceded by two illegible attempts, and for t he first wrote "d," and he made the following explanatory remarks : "I found some difficulty. I always have difficulty with a K ; I always write h ; then I know it is different ; I can't get started somehow with the r, the same with the t. I thought it was simple ;

I took the risk it would come right, and it came right. I wasn't sure until I came to put the stroke and then I found I was right. I had to risk it."

A printed paragraph.—I gave him the following passage from Landor's letters, asking him first of all to read it to himself and then to tell me what he had gathered from it.

"On Wednesday last, I was present at a wedding; the only one I was ever at, except one other. There was bride-cake and there were verses in profusion, two heavy commodities! But what an emblematic thing the bride-cake is! All sugar above, all lumpiness below. But may Heaven grant another, and far different destiny, to my sweet-tempered, innocent, sensible young friend."

Four minutes later he handed the paper back, saying "On Wednesday last I was present at a wedding. The . . . the only one except one other at which I was present. There were . . . presents . . . and verses . . . and bride-cake in profusion. . . . The . . . the bride-cake all sugared above . . . lumpiness below. . . . The one, the cake . . . yes, the cake suggested to be emblematic of the future state of the married couple. . . . I wasn't able to quite follow what was really meant by the emblematic state. There seemed to be in the writer's mind some meaning, but I couldn't find what it really was."

He then re-read the contents silently and wrote as follows:—

"On Wednesday last I was present at a wedding, the only one except one other at which I was present. There were verses in profusion and a brides cake, both heavy commodities. The one all sugar above, all lumpiness below, simmingly an emblem of the future state. May the future state of my innocent young friend be . . ." He ceased to write and said "I've rather lost the trend of things."

He was asked to read the passage aloud, which he did correctly; then he copied it in cursive handwriting clearly and without mistakes.

Finally I asked him "What was it that bothered you?" and he replied, "Well at first it was an ordinary conventional wedding with cake and I suppose in those old days verses; they are not so prevalent nowadays. He seemed to regard the wedding cake as an emblem of the future state of his young friend, who was about to be married . . . and the writer's mind . . . he seemed to . . . regard the wedding cake as . . . as . . as. . . ." Then he gave up all further attempts to explain his meaning.

I demanded what is an emblem? He answered at once "Oh! an emblem is a . . . well . . . the Cenotaph might be taken as an emblem of sacrifice and adhesion to a great principle."

Significance of pictures.—He was given a coloured picture of a motor car standing before a large country house; the driver, a young man, was talking to two girls, one of whom held a greyhound by the collar. Asked the meaning of this picture he went over it in detail from left to right and then back again without the least evidence of constructive appreciation. He said: "There are two trees on the left-hand side and a house, perpendicular columns. There's a doorway on the right and a window just above it. There are chimneys.

Then there are the side windows. Then there are some small buildings at the back, out-buildings or a lodge, something like that. Behind that there are trees. Then there's a small hill; at the bottom of it there's a lake. In the foreground there's a motor car; it's standing. The driver's a man, looks like the owner of the car, not a chauffeur. He is speaking to two ladies. He appears to be addressing more directly a lady with a red hat and another lady standing by is holding a hound." Every detail was recognized correctly; but he did not weld them into a coherent whole and express the meaning of the picture in a set of general propositions.

He was then shown a series of humorous sketches representing a spectator who, arriving late at a play, strips off inadvertently both his coats, and is taking his seat in shirt sleeves to the horrified amusement of the audience. When I asked the patient what he saw in these pictures, he entirely missed the point. "There's an audience, possibly a concert audience. The audience is seated, waiting and . . . a man comes along wearing his coat. He has some difficulty evidently in taking it off, whether real or assumed. The audience seems greatly interested. I'm not sure about it. . . . I was trying to think it might have been part of the performance . . . or he might have got there and seem to be rather prominent. It often happens in a theatre that somebody comes late."

But, on the other hand, he was sometimes surprisingly quick in seeing the point of a picture, if it depended on details, especially if each bore its explanatory label. Thus, I showed him a cartoon of Winston Churchill trying on a hat which was too small for his head; behind on a shelf lay the head-gear appropriate to the Home Office, Board of Trade, Admiralty, War Office, Air Ministry and Ministry of Munitions, each bearing a label. Above stood an unopened band-box marked "The Premier." He said at once, "That, of course, is Mr. Winston Churchill. Shortly, the point is the statesman is suffering from what is commonly called swelled head; his head is too big for his hat. There are many different shapes and the caricaturist has it in his mind that he has worn them all at one time or another. There's the civilian bowler hat, the admiral's peaked hat, the War Office; forage cap it's called in the Air Ministry, the Flying Corps; then the Ministry of Munitions cap, indicated by something connected with the workman, the labourer." Then he returned to the left of the picture and pointing to the first on the shelf said, "This must be a policeman's helmet" (correct); but he entirely missed the hat-box marked "The Premier" and all that it implied.

Comprehension of general significance.—He still showed the same lack of power to grasp the general aim or significance of a question, order, or series of propositions. For instance, on a sunny spring morning I said, before we began work, "I hope you don't find it cold; shall I put the window up?" He answered "Yes," but as soon as I began to raise it he called out "No, no." Then he explained, "When you said 'have the window up,' I thought you meant open . . . more air. You went to put the window like that" (waving his hand upwards) "and I thought no, no, more air, that's what I want."

This is a good example of the confusion which is liable to arise in his dealings with others.

Starting from errors of this kind, he was perpetually liable to arrive at mistaken conclusions. One day he was waiting on the station platform of his native town, when he saw a young lady who was an old acquaintance. His brother told him her name, said she had gone away some time ago and added that she was now married. This the patient strenuously denied, asserting she wore no wedding ring. He had looked for it on what seemed to him to be her left hand, but was in reality her right.

He still had serious difficulty in appreciating the significance of summer time. He gave a perfect definition of summer as " the season at which the sun approaches nearest to the earth and the days are longer and the heat more intense." Asked what he understood by time, he answered "Time is the length of a day reckoned as twenty-four hours subdivided into day and night." He now recognized that summer time consisted in arranging the hands of the clocks on a certain date "so that there may be more day-light during ordinary working hours." But he could not be certain what happened to the clocks. " This bothers me," he said, " very much all through, more especially when we come back again to winter time at the end of the season ; I seem to want to tell you in one clear sentence what happened, when the clocks were altered to normal time ; I seemed to get muddled between two things."

Arithmetic.—He was extremely slow in carrying out the simplest arithmetical exercises and took twenty minutes over the following examples without being able to complete the last one :—

Addition.			*Subtraction.*		
231	648	856	865	782	912
356	326	275	432	258	386
587	974	1131	433	524	26

He brought out the answer to the first sum fairly quickly, but the second caused him extreme difficulty ; he gave it up, but insisted on returning to it later, and finally completed it correctly. The answer to the first subtraction came with moderate ease, but the second was enormously prolonged, and the third of the series was not completed.

He complained "I found difficulty in them all. I found the subtraction more difficult than the addition. When there was a carry, it seemed to be more difficult. What I feel about it is . . . if I were to begin my education, like a boy at school, I shouldn't know where to begin. In those sums you gave me I did the addition almost involuntarily, I think the results of former practice. The subtraction . . . the simplest one, I did it in the more or less involuntary way . . . but with the more difficult I had to think what subtraction really meant."

Coins and their relative value.—Money in all its forms was named accurately and with great rapidity ; even notes were distinguished without fail. But, when he was asked to state the relative value of any two coins, he answered slowly and with hesitation, although he made one actual mistake only in a series of eighteen observations, saying that twelve sixpences went to a shilling.

He still had extreme difficulty in calculating the change he should receive after making a purchase. His tobacco now cost him a shilling an ounce; he would ask for two ounces, placing a two-shilling piece on the counter; if he wanted a box of matches in addition, he waited until the first transaction was over and then took a penny from his pocket, so as to avoid the difficulties of change. Should he happen to have nothing less than a ten-shilling note, with which to pay for his tobacco, he asked the tobacconist to give him florins only (two-shilling pieces); these he counted, "one, two, three, four," and he knew that four was the right number. But, if he was given the change in shillings, he was lost. "I don't like getting a half-crown (two and sixpence) in change; it puzzles me. I know the tobacconist, if he liked, could cheat me."

Drawing.—A glass jug of simple form was placed on the table in front of him and he made a feeble representation of its outlines. Ten minutes later, on attempting to reproduce the jug from memory, he exactly repeated his previous drawing; he was evidently recalling his motor acts and did not rely on his visual images to help him in this task.

Asked to draw an elephant, he produced a scrawl which bore no relation to any known animal; he omitted the trunk and, when I enquired if he had left out anything, he said, "Elephant's nose; I'm not sure where the nose ought to be." I then told him to draw the head only and he became completely confused.

He then said, "I'll draw you a bee-skep" and proceeded to do so accurately, giving the exact form of the Dutch hive they were using, together with the stand and the tin cover to keep off the rain.

Plan drawing and relative position of objects in space.—When removed into another room, he was unable to draw a plan of the one in which we had so often worked; the windows were placed on the wrong side and the relation of the main door to the fire-place was reversed. So far this examination confirmed, but added nothing to, my previous observations. But from this point onwards I modified my procedure as follows. I made him shut his eyes and point to the position of the various objects as I named them, which he did perfectly. His eyes were then opened and I put before him an outline plan, on which he indicated with his finger the place of the various pieces of furniture; this he carried out correctly in every instance. Finally, I asked him again to draw a plan of the room in which we worked and he was now able to do so, at any rate as far as its main features were concerned. He said, "When you asked me to do this first I couldn't do it. I couldn't get the starting point. I knew where all the things were in the room, but I had difficulty in getting a starting point, when it came to setting them down on a plan. You made me point out on the plan and it was quite easy, because you had done it. After things were pointed out, I retained them in my memory and got them down on paper quite easily."

Visual images.—A few days, after I had tested his power of drawing, he volunteered the following introspective remarks: "I thought of what you asked me to do, drawing the glass. In bed I was trying to think about it. I was trying to see the glass bottle; the picture seemed to evade me. I knew it was a bottle and I could describe the shape of it, and I remember making a drawing of it, and I could describe the drawing. But then, when it came to seeing it as a picture, I was more or less nonplussed. I often seemed to have got the picture, but it seemed to evade me."

"There is a photograph of my wife, which is hanging in the bedroom. I can see that; the expression in that photograph is very good, I can see that."

"I can see the bee alighting on the alighting board. I see it quite clearly. Now, for instance, our hives are painted in two colours, one green, one white. I can see a bee alighting on the alighting board, say, for instance, yellow-coloured pollen. Yes, I can see that quite clearly."

"The more I try to . . . to make them come the more difficult it is to get in touch with them, as one might say."

Orientation.—He was completely unable to find his way alone. He never took his bearings and, if he was going to a place for a second time, did not recognize landmarks or appreciate that he was passing over the same ground again. He did not know which way to turn, and if he chanced to take the opposite side of the road, became confused and was ignorant in which direction to walk.

Given the number of a turning to the right or left, he could never find it correctly; but, told to take the "next on this side," he was able to do so. Left and right puzzled him greatly; he tried to work them out by thinking which was the left half of his body and frequently brought out an incorrect answer.

Relation of objects to one another.—His inability to remember the relation of external objects to one another came out, when he was given a mechanical task. He made the four portions of a bee-hive under supervision of the instructor, but was unable to put them together. He was incapable of wiring his bee-frames except by passing the wire backwards and forwards in direct sequence from side to side.

I placed before him all the breakfast utensils requisite for one person, and asked him to set the table. He quickly placed the cup, the saucer and the plate correctly. Then he became confused, laid the knife across the plate and removed it, set the spoon to the right of the plate and took it away again; finally, after much hesitation, he placed the fork to the left, the knife to the right and the spoon above the plate. Subsequently he set the remaining objects such as the sugar basin, salt-cellar and pepper-pot in their appropriate positions.

He explained his difficulty in carrying out the task as follows: "There was something missing, something unusual. I got the knife and fork, I couldn't find . . . let us say the bacon and eggs. Then the spoon puzzled me; I wasn't quite sure why it was there. If I was laying my own breakfast table I should know, because I always take porridge. If I saw the spoon, I should look for the bowl for the milk and so on; but there seemed nothing like that, and so I thought the best way out of the difficulty was to place the spoon in a position in which it might be convenient for any purpose."

"I always try to have the things in my bedroom in exactly the same position. If I've got to think where they are and look for them, I get muddled; I lose time. I have them all in the same order; then I don't have to think. If I have to look for them I am bothered. If I go to a strange room, it's a more difficult job to dress and takes an appreciably longer time than if I am at home."

Games and puzzles.—He could not play any games or amuse himself with puzzles. I played draughts with him, simplifying the game by removing one of the three rows of men on either side. He complained, on being beaten with the greatest ease, "The chief bother was trying to follow the consequences of the next move. I couldn't foresee what would happen."

He had never been good at billiards and now could not play at all. "Somehow the three balls put me out of it. Even with two balls my stroke was indifferent, but if I wished to cannon I seemed to think of the three actions necessary to be made. As a consequence I became muddled, I couldn't make a cannon. A straight shot with two balls was not so bad, but the third ball confused me. I seemed to think of the three functions at the same time and got muddled."

I therefore tried the following experiment. A basket was placed at the end of the room and he threw balls of paper into it, even more accurately than I could; but, when I placed a screen in front of it, his shots became extremely bad, and he said "When I could see the basket, I could follow the line of vision; when it was covered, I didn't seem to feel so confident it was in the same place, I don't know why. I'd seen the basket before you'd put the screen there; I knew you hadn't changed the position, but in some odd way I didn't feel perfectly confident in my own mind that it was in that position."

Serial Tests.

(1) *Recognition and naming of common objects.*—All these tests, except that of writing the name of an object shown to him, were now carried out perfectly. His handwriting had greatly improved, he spelt the words correctly, but still tended to hurry as if he were afraid of forgetting what he had to do. During these observations he said, "I felt quite confident. But there was an odd thing the other day. I was down at carpentry; the man had different bits of wood, he was going to number them. I couldn't make the A and the C; I made the B, I couldn't make the D."

Thus in spite of his perfect writing he is still uncertain about the formation of individual letters to command; this corresponds with the results obtained when he was made to write the alphabet.

(2) *Recognition and naming of colours.*—He carried out all these tasks without any material mistake, but evidently found some difficulty in writing the names of the colours, although he spelt them correctly. This he explained

as follows: "The only difficulty had nothing to do with the colours. You called it violet; I named it mauve. The same with orange; the colour was quite familiar, but the term orange did not seem to come to me. I compromised by calling it light brown, which was not quite the correct colour. But, when you said orange, I was quite certain that it was orange." Whenever he was in doubt, his handwriting deteriorated and he formed the word hurriedly.

(3) *The man, the cat and the dog test.*—He was already able to carry out this test perfectly in June, 1919, and the records obtained in May, 1921, were equally good.

At the close of these observations he volunteered the following statement: "I can see a man with his trousers cleanly cut. He is tall and straight; he has a hat on, and is clean-shaven." I said, "Tell me about the dog." He answered, "The dog has short legs, like a terrier, roughish coated; maybe a Scotch terrier." Q: "Now about the cat?" A: "It's an ordinary cat; the whiskers are rather evident. I think she is sitting, not lying down; but a cat rests on her hind legs, the position a cat has when she's. . . . Her weight is on that part of her . . . it corresponds to our . . . let me see . . . the femur isn't it? She's just sitting up, on her haunches, that's the word I wanted."

(4) *The clock tests.*—(See Table VI.)

Direct imitation was carried out exactly, and he set the hour hand in a position proportionate to the minutes. Oral and printed commands were badly executed, he made many mistakes, mistook the hands, and was slow, hesitating, and uncertain of the correctness of his final choice. Commands given in railway time yielded better results, especially if they were printed; he held the card before him until he had finished setting the clock, looking back repeatedly for correction and reassurance. He said, "It was much easier; I could get a starting point. You see the main thing that really mattered was the unit, two o'clock: the other matters were subsidiary." Thus, when the order was given in railway time, he set the hour and then the minutes; whereas if these preceded the number of the hour, as with the ordinary nomenclature, he became confused. He could now both tell the time and write it correctly.

(5) *The coin bowl test.*—In June, 1919, his answers to verbal commands were slow and somewhat uncertain, but finally correct. He made no mistakes and was quicker and more certain to printed commands; but he held the card in his hand and repeatedly referred to it for confirmation.

By May, 1921, all hesitation had disappeared and this test was carried out perfectly. "I have practically no difficulty. I take the penny and I say 'first into third' (no word is uttered). I just consider for a moment and then I get it."

(6) *The hand, eye and ear tests.*—(See Table VII.)

He still had difficulty in imitating movements made by me, or represented pictorially. Reflection in the glass did not materially improve his answers. Oral and printed commands, carried out silently, gave better results and, when

TABLE VI.

	Direct imitation	Oral commands		Printed commands		Telling the time	Writing down the time	
		Ordinary nomenclature	Railway time	Full words	Railway time		In words	In railway time
5 minutes to 2 ..	Correct	Reversed hands. Long hand at 2	Correct	Set 2.5	Correct	Correct	Correct	Correct
Half past 1 ..	,,	Slowly, correct	,,	Correct	,,	,,	,,	,,
5 minutes past 8..	,,	Reversed hands. Long hand at 8	,,	Hour hand between 7 and 8: Long hand at 5 minutes past	,,	,,	,,	,,
20 minutes to 4 ..	,,	Set 4.20	Set 4.20	Set 4.20	,,	,,	,,	,,
10 minutes past 7	,,	Both hands at 7	Correct	Correct	,,	,,	,,	,,
20 minutes to 6 ..	,,	Hour hand at 6. Otherwise correct	,,	Correct (very slow)	,,	,,	,,	,,
10 minutes to 1 ..	,,	Correct	Reversed hands. Long hand at 12	Correct	,,	,,	,,	,,
A quarter to 9 ..	,,	,,	Correct	,,	Hour hand at 8. Long hand correct	,,	,,	,,
20 minutes past 11	,,	,,	,,	,,	Correct	,,	,,	,,
25 minutes to 3 ..	,,	Set 3.25	Set 2.25	Hour hand at 3. Long hand correct	,,	,,	,,	,,

TABLE VII.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Pictorial commands	Pictorial commands reflected in a mirror	Oral commands	Printed commands	Reading aloud and executing printed commands		Writing down movements made by the observer
							He read	Movements made	
L. hand to L. eye	Correct	Correct	Correct	Correct	Correct	Correct	Correctly	Correct	Right hand to left eye
R. hand to R. ear	,,	,,	,,	,,	,,	,,	,,	,,	Reversed
R. hand to L. eye	,,	,,	L. hand to L. eye	,,	,,	Reversed	,,	,,	,,
L. hand to R. eye	L. hand to R. *ear*	R. hand to R. eye	Correct	R. hand to R. eye	,,	Correct	,,	,,	,,
L. hand to L. ear	Correct	Correct	,,	Correct	,,	,,	,,	,,	,,
R. hand to R. eye	,,	,,	,, (slow)	R. hand to R. *ear*; corrected	,,	,,	,,	,,	Correct
L. hand to R. ear	,,	L. hand to L. ear	,,	R. hand to R. ear	,,	,,	,,	,,	Reversed
R. hand to L. ear	L. hand to L. ear	Correct	,,	R. hand to R. ear	,,	,,	,,	,,	Correct
L. hand to L. eye	L. hand to R. eye	,,	L. hand to L. *ear*	Correct	L. hand to R. eye	,,	,,	,,	Reversed
R. hand to R. ear	Correct	,,	Correct	,,	Correct	,,	,,	,,	Correct
R. hand to L. eye	,,	L. hand to L. eye	Reversed	,,	L. hand to L. eye	,,	,,	,,	,,
L. hand to R. eye	L. hand to L. eye	Correct	,,	R. hand to R. *ear*	Correct	,,	,,	,,	,,
L. hand to L. ear	Correct	,,	Correct	Correct	,,	,,	,,	,,	,,
R. hand to R. eye	,,	,,	R. hand to L. eye	,,	,,	,,	,,	,,	,,
L. hand to R. ear	,,	R. hand to R. ear	Reversed	R. hand to R. ear	,,	,, (slow)	,,	,,	,,
R. hand to L. ear	R. hand to R. ear	Correct	R. hand to R. ear	L. hand to L. ear	,,	Correct	,,	,,	,,

he was allowed to read the order aloud, he executed it without fail. Writing down the movements made by me gave him considerable trouble; he was slow and hesitating and made several mistakes.

Condition seven years after the Injury (*February* 27 *to March* 5, 1923).

He took a cottage in the West of England in order to carry on his business of bee-keeping. At first all went well and he was happy; but gradually the strain and worry of the hard work began to tell upon him. The little house was badly constructed and the winter storms beat upon its tin roof like hail, preventing him from obtaining a sufficient amount of sleep. The new hives, ordered from the makers to an exact measure, deviated from scale and could not be readjusted; this troubled him greatly. Finally, the bees turned out to be infected with disease; they had to be destroyed and all the capital and labour expended by the two young people were lost.

Throughout this year he steadily deteriorated and on August 25, 1922, was seized with an epileptiform attack whilst in bed; he lost consciousness, became rigid, but there was little "jerking." He did not bite his tongue or pass urine. This fit was followed by greatly increased "nervousness" and tendency to confusion. The weather was extremely bad and he went out of doors very little; sleep deserted him and he ceased to take sufficient food. Finally he and his wife were forced to give up the experiment with the close of the year.

When I saw him in February, 1923, the wound was in perfect condition, firmly covered with tough scar tissue, painless and not tender to the touch; it did not pulsate. The discs were unaffected and there were no abnormal physical signs of any kind, apart from his disorders of speech.

Articulated speech was not affected except that he tended to become confused and to pause in narration like a man who has lost the thread of what he wanted to say. Verbal formation and syntax were perfect. He could name common objects, geometrical shapes or colours without difficulty and repeated everything said to him with ease.

Understanding of spoken words.—He was still in exactly the condition described on p. 511. He chose any object shown to him with certainty and even carried out the hand, eye and ear tests to oral commands. But he made many mistakes in setting the hands of a clock, provided the order was given in words; if however it was in the form of numbers, the so-called railway time, he executed it correctly.

This tendency to confusion was even more apparent in general intercourse; but, in spite of these misunderstandings, he gave repeated evidence of considerable powers of appreciation.

Reading.—He still had considerable difficulty in grasping the full significance of what he read to himself, although he could choose common objects, geometrical shapes and colours accurately to printed commands. The hand, eye and ear tests were executed slowly but correctly, and yet he made many errors in setting the hands of a clock, when the order was given in the usual nomenclature. On the other hand commands in railway time were carried out with no mistakes though sometimes slowly.

He read aloud perfectly; enunciation and rhythm were normal and he was able to understand the meaning of printed sentences better, if he was permitted to articulate the words.

Writing.—He still wrote with great rapidity, as if he were afraid of forgetting what he intended to place upon paper, and his handwriting suffered in consequence. Name and address were written correctly and he composed a letter of considerable length, which was on the whole remarkably coherent.

He wrote well to dictation and copied accurately from print, but his handwriting was hurried and poorly formed.

The alphabet.—He could say the letters in correct sequence, repeat them after me and read them aloud perfectly. But, when he attempted to write the alphabet, he was liable to become confused. Thus he wrote: *a b b c d e f g h s* *i* *j k*. The remainder were written correctly. At the end he said, "I made a mistake there" (pointing to the letter preceding *c*), "I was conscious of it; I had *c* in my mind's eye; I went to make it, but it seemed to act of its own accord and I went wrong. With *i*, just the same sort of thing occurred; I couldn't get on with the *j* properly and I put a capital, which seemed to come easier." It is noticeable that he wrote each letter very quickly, as if afraid of forgetting what he wanted to write. To dictation he made exactly the same mistakes, writing *a b b c d e f g H i h j i j k*, &c. Even when copying from printed capitals he wrote *j i* for I, and *s j* for J, although the other letters were correctly transcribed in cursive script. Given the twenty-six block letters, he put them together in the right sequence saying: "That's quite easy because I do one thing at a time; I know what ought to come next and seeing the letter confirms it."

A printed paragraph.—I selected the following description from Dickens, to serve as a test: "The gentleman spoken of had a very ugly squint and a prominent chin. He was wearing a tall white hat with a narrow flat brim and riding breeches with yellow leather gaiters. He carried in his hand a switch, with which he tapped his boots, as he talked in a hoarse voice."

Asked what he had understood, after reading these sentences silently, he replied: "The passage tells of a peculiar looking man. He had a prominent chin and an ugly squint. He wore riding breeches and yellow gaiters. He carried in his hand a switch, with which he tapped his riding breeches . . . his gaiters . . ."

He read this paragraph through once more to himself and wrote down the following account: "The gentleman spoken of had a prominent chin and an ugly squint. He wore riding breeches and yellow gaiters. He carried in his hand a switch with from time to time he tapped his riding." The spelling was correct but the writing was bad and became worse towards the end; two words were omitted in the last sentence.

These sentences were read aloud from print perfectly and he both copied and wrote them to dictation without error or omission; but the writing was hurried and poor. During the act of copying he said, "Sometimes when I'm writing, I don't form a letter properly, and when I go back over it again, I get puzzled . . . from the fullstop the continuity is lost and the writing doesn't flow easily."

I then asked him to narrate to me what he remembered of the paragraph he had so often read and transcribed. He replied, "The gentleman spoken of had a prominent chin and an ugly squint. He wore . . . he wore riding breeches and yellow gaiters. . . . He . . . carried in his hand a switch . . . with which . . . from time to time . . . he rapped . . . his riding boots. There's another point I have left out; he wore a tall hat with a narrow flat brim . . . There is still another piece. . . . It's all chopping and changing. . . . I have forgotten pieces of it and things occur to me as I go over it again."

I then handed him a list of the various details mentioned in this description, arranged in a vertical column (ugly squint; prominent chin; tall white hat; narrow flat brim; riding breeches; yellow gaiters; carried a switch; tapped his boots; talked in a hoarse voice). The whole set were reproduced correctly from memory, although in changed order. In fact, his memory tested in this way was remarkable and he explained, "If I get them in any order, just as recollection comes to me . . . as soon as a word comes to me, I must grasp it in case it escapes me."

Numbers and arithmetic.—He counted accurately and without hesitation, each number following its predecessor in rapid sequence.

He still found great difficulty in carrying out simple exercises in arithmetic, and his answers, even when correct, were given slowly and with hesitation:—

Addition.			*Subtraction.*		
231	648	856	865	782	912
356	326	375	432	258	386
587	974	1131	433	544	524
				(wrong)	(wrong)

Coins and their relative value.—Coins and notes were named accurately and he was now able to state their relative value without mistakes, although he was somewhat slow and uncertain. But he still found much difficulty with change in the transactions of daily life.

I gave him a ten-shilling note and asked him to pile up its equivalent from amongst the coins on the table; this he carried out with some effort correctly. I then handed him the same note, and telling him I had bought something for two-and-six, asked for change. This puzzled him greatly; for although he said "seven-and-six," he had great difficulty in collecting the coins to make up this sum. I gave him the same note once more and said I had purchased something for "three-and-three;" this he was entirely unable to work out. He complained, "It is parts of a shilling that bother me and a halfpenny makes it worse; I get confused and lose the significance of the figures."

Drawing.—When a painted jug was placed before him he made a recognizable outline drawing, poorly executed and omitting the pattern. The lines were feeble and uncertain, and a child could have done better.

A quarter of an hour later he reproduced it from memory with the same faults and omissions, saying, "I can see the jug in front of me as I draw it. I can see the general shape, the colours; there's blue and green and an eastern colour. I didn't take notice of the pattern. Then there was the shape of the jug, a sloping shape, wider at the base than further up. The lip was slightly broken. Then there was the handle, an ordinary old-fashioned handle, except that there were one or two excrescences or rather knobs." All these details were absolutely correct, but they were not represented on his drawing; in fact, this is another example of his remarkable power of remembering isolated aspects of some object or event without the ability to combine them into a general whole.

Asked to draw an elephant, he produced a childishly inadequate body and legs, and was hopelessly puzzled over the head. He said, "It's awfully different; it's hard to work in the details, to find where the details ought to go." But when I drew an outline of the animal, leaving blank the eye, ear, trunk and mouth, he inserted all but the ear correctly, naming them as he did so.

Told to draw anything he liked, he made an excellent outline picture of a Dutch beehive, pointing out the high entrance which distinguished it from the English form, and indicated the bees on guard before the opening.

Memory and images.—There can be little doubt that he still retained considerable powers of visual imagery, although he could not always employ it at will for the purposes of language. He not only described to me the colour and form of the jug given him as a model, but when I asked him, "Do you remember the man, the cat and the dog I showed you yesterday?" he replied as follows: "Yes, a tall thin man; I think he had a tall hat; I see him, but I'm not clear of other details. He must be clean shaven . . . he had ordinary trousers . . . I can't remember any detail about his coat. The dog . . . the dog was a short thick-set type of dog, something like an Aberdeen terrier . . . There was shading on the picture to show his rough coat . . . I think he was looking to the left. The cat was sitting on her haunches . . . she had the usual . . . the usual prominence was given to her whiskers." I asked if he could see them clearly, and he answered, "Yes, I can see the cat sitting, and the shaggy dog, and the man . . . yes."

He frequently gave evidence of a startling memory for detail; for instance, set to write me a letter, he remembered what he had written some years before and amplified it on the second occasion. He visited a friend who had been a fellow officer in the same regiment, and astonished him by an extensive memory of the men's names and peculiarities. Even when he did not know the name, he could describe the man sufficiently accurately to be recognizable. His mind contained a mass of detail which he had difficulty in utilizing for the logical sequence of a general statement.

Significance of pictures.—These tests revealed the same difficulties as before, and he entirely failed to appreciate the meaning of the humorous picture of the

TABLE VIII.

	Direct imitation	Oral commands		Printed commands		Telling the time	Writing down the time	
		Ordinary nomenclature	Railway time	Ordinary nomenclature	Railway time		In words	In railway time
5 minutes to 2 ..	Correct	Correct	Correct	Set 5 minutes to 10	Hour hand at 1 ; long hand at 55 min.	Correct	Correct	Correct
Half-past 1 ..	,,	,,	,,	Correct	Correct	,,	,,	,,
5 minutes past 8..	,,	Gave up puzzled	,, (slow)	Long hand correct ; hour hand between 7 and 8	,,	,,	,,	,,
20 minutes to 4 ..	,,	Set 4.20	,,	Correct	,,	,,	,,	,,
10 minutes past 7	,,	Very slow ; finally correct	,, (slow)	,,	,,	,,	,,	,,
20 minutes to 6 ..	,,	Set 6.35	,,	Correct (very slow)	,,	,,	,,	,,
10 minutes to 1 ..	,,	Correct	,,	Correct	,,	,,	,,	,,
A quarter to 9 ..	,,	,,	,,	,,	,,	,,	,,	,,
20 minutes past 11	,,	Long hand at 20 to ; hour hand at 11	,,	,,	,,	,,	,,	,,
25 minutes to 3 ..	,,	Correct	,,	Long hand correct ; hour hand between 3 and 4	,,	,,	,,	,,

TABLE IX.

	Imitation of movements made by the observer	Imitation of movements reflected in a mirror	Pictorial commands	Pictorial commands reflected in a mirror	Oral commands	Printed commands	Reading aloud and executing printed commands		Writing down movements made by the observer
							He read	Movement made	
L. hand to L. eye ..	Correct	Correct	Reversed	Reversed	Correct (slow)	Correct (slow)	Correctly	Correct	Correct
R. hand to R. ear ..	,,	,,	Correct	,,	,,	,,	,,	,,	,,
R. hand to L. eye ..	Reversed	,,	,,	,,	,,	,,	,,	,,	,,
L. hand to R. eye ..	Correct	R. hand to R. eye	,,	,,	,,	,, (slow)	,,	,,	,,
L. hand to L. ear ..	,,	Correct	,,	Correct	,,	,,	,,	,,	,,
R. hand to R. eye ..	,,	,,	,,	R. hand to R. *ear*; corrected	,,	R. hand to R. *ear*; corrected	,,	,,	,,
L. hand to R. ear ..	R. hand to R. ear	R. hand to R. ear	,,	Correct	,,	Correct	,,	,,	,,
R. hand to L. ear ..	Correct	Correct	,,	,,	,,	,,	,,	,,	,,
L. hand to L. eye ..	Reversed	,,	,,	,,	,,	,,	,,	,,	,,
R. hand to R. ear ..	Correct	,,	,,	,,	,,	,,	,,	,,	,,
R. hand to L. eye ..	L. hand to R. *ear*	,,	Reversed	,,	,,	,,	,,	,,	,,
L. hand to R. eye ..	Reversed	,,	Correct	,,	,, (slow)	,,	,,	,,	,,
L. hand to L. ear ..	,,	,,	,,	,,	,,	Correct (slow)	,,	,,	,,
R. hand to R. eye ..	,,	,,	,,	,,	,,	,,	,,	,,	,,
L. hand to R. ear ..	,,	,,	,,	,,	,,	,,	,,	,,	,,
R. hand to L. ear ..	,,	,,	,,	,,	,,	,,	,,	,,	,,

man who inadvertently removed his two coats on entering a theatre. He added, "Apparently there's a joke somewhere, but I haven't been able to see what it really is."

Orientation and plan-drawing.—He still had extreme difficulty in finding his way, and, although he had passed down a street many times, he never recognized which turning to take. When travelling by the Underground Railway, his wife was obliged to push him off the moving staircase; for he was always completely puzzled how to step from it at the end.

Another set of observations to test his power of drawing a plan, carried out in the same order, brought out exactly similar results to those described on p. 516.

Serial Tests.

(1) *Recognition and naming of common objects* and

(2) *of colours* were carried out perfectly and the names were written down without mistakes.

(3) *The man, cat and dog tests* gave him no difficulty.

(4) *The clock tests.*—(See Table VIII.)

This table shows a remarkable resemblance to that obtained two years before (p. 520), ample testimony to the trustworthiness of the tests. He could tell the time and write it down correctly. Oral and printed commands still gave him considerable difficulty if presented in ordinary nomenclature, but could be executed, though slowly, if the order was in railway time.

(5) *The coin-bowl test* was performed without mistakes.

(6) *The hand, eye and ear tests.*—(See Table IX.)

Although the actual results were somewhat better these records corresponded closely to those obtained two years before (p. 521). He had regained some further power to imitate my movements and to perform pictorial commands: but he was still puzzled when they were reflected in the glass, and, although the actual errors were not numerous, his actions were slow and uncertain. He could, however, write down my movements without fail.

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NOTICES OF RECENT PUBLICATIONS.

Handbuch der Neurologie. Von M. LEWANDOWSKY. Ergänzungsband, Erster Teil. Berlin: Julius Springer. 1923. Price 20s.

This, the first part of the supplementary volume of Lewandowsky's "Handbuch der Neurologie," is concerned with subjects on which our knowledge has been enriched by the experiences of the war. It contains five separate articles. The first, by Birnbaum, is devoted to the special forms of the psychopathies and psychoses observed during the war, particularly to their nature and their direct and indirect causal factors. Many of the conclusions are important, as that there is no evidence that the strain of war or even head injuries received during it have had any influence on the origin or course of general paralysis and other organic insanities. The war has apparently led to little or no increase in insanity in Germany, a fact which indicates that many exogenous factors on which much weight has been laid are of little or no importance. The influence of the war is seen in the increase of hysterical rather than psychiatric manifestations, and the tendency of the latter to assume hysterical features.

In the following sections Bumke deals with the neuroses of war, Lange with their treatment, and Kehrer with the symptomatology of hysteria and neurasthenia. Bumke's short article on the nature of the neuroses is extremely interesting; he denies that subconscious factors play any important part in their pathogenesis. Kehrer's section contains little that is new, though he records many rare and curious symptoms. Lange reviews the many methods of treatment that have been tried. Hypnotism has been apparently much employed in Germany, but emphasis is also laid on the value of suggestion in various forms, isolation and regulated work. By these methods 90 to 95 per cent. of cures have been obtained, but recurrences often occurred during the war. Psycho-analysis is rarely required or of use.

Redlich's article on epilepsy is mainly a review of the literature of the last ten years on this disease. As he concludes that military service has had little or no influence on epilepsy, it is with the disease as seen in ordinary circumstances that he mainly deals. There is, however, an interesting chapter on epilepsy following gunshot wounds of the head.

Einführung in die Klinik der inneren Sekretion. Von G. PERITZ. S. 257, mit 31 Abbildungen. Berlin: S. Karger. 1923. Price M. 4.80.

The author's aim has been to provide a concise textbook which may, on the one hand, serve as an introduction to the fuller study of the complicated functions of the ductless glands, and on the other suffice for the needs of the ordinary student. He has produced a readable and useful volume in which both the clinical and physiological aspects of the subject receive due attention, and yet are not overladen by detail.

The various endocrine organs are dealt with in separate chapters. Some of the features which attract attention are a discussion on the nature and causes of infantilism, the aberrance in the sexual functions due to affections of the genital glands, and the physiology of the parathyroids and their relation to spasmophilic conditions. The functions of the hypophysis are also adequately discussed and its diseases referred to, though from a general rather than from a neurological point of view. A discussion on the influences of the various internal secretions on the nervous system constitutes one of the most interesting chapters: a list of the pharmacological and other tests of their activities which is included in it also deserves mention.

Almost all the illustrations are of clinical subjects. There is no bibliography or even references to the authorities cited, but the book is provided with a good index,

An Outline of Psychology. By WILLIAM McDOUGALL. Pp. 456. London: Methuen and Co. 1923.

The professed objects of this book are to give the student new to psychology a profitable line of approach, a fruitful way of thinking of psychological problems, and a terminology as little misleading as possible. But it is not to the uninitiated student only that this textbook will appeal; all interested in psychology will scan its pages with interest and profit, though they may not agree with all Professor McDougall's methods and conclusions.

He insists from the first page of his preface to the last chapter of his book that the "stream of consciousness" cannot be regarded as consisting of discrete parts or atoms of conscious stuff, each of which may be in some way or other attached or related to an elementary process in the brain, and the associations of which can be explained by the laws of the physical and chemical sciences. Consequently in psychology the student cannot rely on the methods of observation and reasoning which he has been taught to apply to the physical world, in which all events are regarded as links in a mechanical chain of cause and effect. In the mind a "purposive striving" is the fundamental category, and its process is radically different from the laws of mechanical sequence. His main effort is, therefore, to break loose from "the tradition of mental life as a mechanical mosaic," and he consequently treats his subject in a manner unlike that which it has received in most of the current textbooks of similar scope in our own and in other languages.

His methods and arguments will not receive universal acceptance, and in certain points will certainly excite controversy, but whether we agree with them or not we must admit that this book is a logical and vigorous presentation of one point of view. The style is as concise and clear, and at the same time as cogent, as we have learned to expect from the author's previous books. A second volume which will treat abnormal mental processes on the same lines is promised.

Papers on Psycho-analysis. By ERNEST JONES. Third edition. London: Baillière, Tindall and Cox. 1923. Price 25s.

This well-known collection of papers on Psycho-analysis remains substantially unaltered. No fundamental changes in view are discernible, though some ideas obscure and undeveloped in earlier Freudian writings are here further elucidated and developed.

The main advances, as illustrated in this book, lie in the region of so-called Ego psychology. This development is all to the good, seeing that the earlier insistence on the sexual causation of the neurosis and of character formation rendered the theory difficult of acceptance by psychologists brought up in schools where the unifying effect of the Ego in the shaping of the mental life remains a matter of some importance.

Of the newer essays the most valuable to the student of Freudian psychology are "Some Problems of Adolescence" and the "Nature of Autosuggestion." The application of psycho-analytic principles to the study of the psychoses receives further notice in various parts of the book.

Common Symptoms of an Unsound Mind. By G. RUTHERFORD JEFFREY. Foreword by Sir James Crichton-Browne. Pp. xviii + 264. London: H. K. Lewis. 1923. Price 7s. 6d.

This book is avowedly written for the general practitioner, but even if this is its only aim, it is distinctly disappointing.

Dr. Jeffrey begins with delusions, which he defines merely as "false beliefs"; there is no attempt at their explanation or reference to their biological and clinical importance, and to their relationship to myths, dreams, religions and folklore. True the author mentions the "subconscious mind," but without the slightest indication of what he means by the term, and without defining its scope and functions. Dementia præcox is divided into two groups, one with and the other without delusions, a somewhat novel classification.

Paranoia is constantly referred to as a disease in which the pathology is quite unknown, which is a very sweeping and inaccurate statement. Hallucinations are loosely described, and nowhere is the mechanism of projection mentioned. The author describes simple mania and melancholia as clinical entities distinct from manic-depressive states, and having a better prognosis. The very clear conceptions of Kraepelin and others of manic-depressive states do not seem to be appreciated by him. He rightly lays stress on the differences in the character of the excitement in such varying states as the manic phase of manic-depressive insanity, confusion and general paralysis. But the practitioner is scarcely likely to learn these differences when he can rely much more certainly on the cytology and chemical reactions of the cerebro-spinal fluid. Lumbar puncture as a means of diagnosis does not appear in the volume. There are other serious omissions. There is no mention of presenile states of depression (true melancholia) nor of the neuroses and psychoneuroses, conditions which the practitioner meets more frequently. Arsenic as a possible cause of Korsakow's syndrome is worthy of mention in view of its recent prominence.

In tho article on testamentary capacity, there are no practical directions to guide the practitioner in the examination of a person whose will, for instance, might be disputed.

The Psychology of Education. By D. KENNEDY-FRASER. London: Methuen and Co., Ltd. 1923. Price 6s. 6d.

It would be impossible for the lay reader to gain any idea of the scope and methods of Modern Educational Psychology by a reading of a large textbook or articles in the Journals. He would be immediately appalled by the discussions on the nature of general intelligence, and the detailed mathematical analysis of correlations. Dr. Fraser has designed his book in order to introduce the uninitiated into the methods of psychological investigation in so far as they concern education. Part I is a clear statement of the methods of investigating intelligence by the now familiar tests and their modifications. While the exposition of method and application leaves nothing to be desired, one would like to have an even elementary discussion of the controversial side of the problems of the intelligent quotient, and the way in which such quotients are capable of modification by more rational and sympathetic treatment of apparently backward children. The author wisely does not go into the vexed question of general intelligence.

The rest of the book covers the whole field of psychological development under the head of the various psychological functions, and the subject is throughout treated from the point of view of the development of the child mind. So many textbooks of psychology are in the habit of treating mental development in the abstract that this approach is very refreshing. The object of the book is to prove that by experimental discovery of the type of reaction to which the child belongs better results in education can be achieved, so that having discovered the path along which development in a particular case normally moves, more rapid and valuable progress can be obtained.

The Constitutional Factors in Dementia Precox. By N. D. C. LEWIS. New York: Nervous and Mental Disease Monographs. No. 35. 1923. 3.60 dollars.

The author, after a brief account of the history and psychological make-up of the patient, gives a detailed report of the pathological findings in the viscera in general, and of the circulatory system and endocrine glands in particular, in twenty-two cases of dementia præcox. The heart shows arrested development at the pubescent stage, diminished connective tissue displacement, and the muscle fibres are small though normal. In the aorta there is frequently a thinning of the intima, but the media is denser in structure than in organic disease of the arteries. He regards this condition as similar to that found in the status lymphaticus syndrome, a condition frequently met with in dementia præcox.

The most striking endocrine changes occur in the testicles, thyroid and adrenals. There again the changes suggest a regressive phenomenon, or rather developmental arrest at the puberty stage, but there is always sufficient glandular structure left to permit the emergence of secondary sexual characteristics.

In the fact that these three glands have been associated with the emotional disposition of individuals he sees at least a point of contact between the physical state and the psychological picture of dementia præcox. Further, on the psychological side one of the features is what psychologists speak of as the regressive type of mentality.

Observations et Expériences de Psychologie Scolaire. Programmes des Ecoles Normales. By M. FONCAULT. Paris: Les Presses Universitaires de France. 1923. Price 5 francs.

Professor Foncault's little handbook is a concise account of the methods of investigation of the minds of children in the Ecoles Normales.

In the space of 150 pages he covers the whole field of experimental psychology as applicable to school children of all ages. The opening chapters are psycho-physiological, that is concerned with the physical functions and the organs of sense. Thence he passes on to consider memory, mental fatigue, judgment, reasoning and language, with their modifications at various times in the school day.

Complex activities such as imagination, dreaming, character and temperament are fully considered. There is no concession made to transcendental psychology, the whole being considered from the experimental point of view with just those introspective notes which make observation complete. He is fully alive to the difficulty of making a reliable diagnosis of intellectual capacity from mere routine examination by tests during school hours, and recognizes that a proper judgment of character can only be obtained by personal appreciation on the part of those persons who are in constant contact with the children, as the parents and teachers.

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